Devi, S.
08/870762

FILE 'REGISTRY' ENTERED AT 12:08:22 ON 16 MAY 2006

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 15 MAY 2006 HIGHEST RN 884382-45-0
DICTIONARY FILE UPDATES: 15 MAY 2006 HIGHEST RN 884382-45-0

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH January 6, 2006

Please note that search-term pricing does apply when conducting SmartSELECT searches.

****
* *
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added, *
* effective March 20, 2005. A new display format, IDERL, is now *
* available and contains the CA role and document type information. *
* *
****

Structure search iteration limits have been increased. See HELP SLIMITS for details.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

L1 14 SEA FILE=REGISTRY ABB=ON PLU=ON KCNTATCATQRLANFLVHSSNNFGP ILPPTNVGSNTY/SQSP

L1 ANSWER 1 OF 14 REGISTRY COPYRIGHT 2006 ACS on STN
RN 865891-48-1 REGISTRY
CN L-Tyrosine, L-lysyl-L-cysteinyl-L-asparaginyl-L-threonyl-L-alanyl-L-threonyl-L-cysteinyl-L-alanyl-L-threonyl-L-glutaminyl-L-arginyl-L-leucyl-L-alanyl-L-asparaginyl-L-phenylalanyl-L-leucyl-L-valyl-L-histidyl-L-seryl-L-seryl-L-asparaginyl-L-asparaginyl-L-phenylalanylglycyl-L-prolyl-L-isoleucyl-L-leucyl-L-prolyl-L-prolyl-L-threonyl-L-asparaginyl-L-valylglycyl-L-seryl-L-asparaginyl-L-threonyl- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 255: PN: US20050215475 SEQID: 257 unclaimed protein
CI MAN
SQL 37

SEQ 1 KCNTATCATQ RLANFLVHSS NNFGPILPPT NVGSNTY
========== ========== ========== =======
HITS AT: 1-37

RELATED SEQUENCES AVAILABLE WITH SEQLINK

REFERENCE 1: 143:353335

L1 ANSWER 2 OF 14 REGISTRY COPYRIGHT 2006 ACS on STN
RN 856043-00-0 REGISTRY
CN L-Tyrosine, L-lysyl-L-cysteinyl-L-asparaginyl-L-threonyl-L-alanyl-L-threonyl-L-cysteinyl-L-alanyl-L-threonyl-L-glutaminyl-L-arginyl-L-leucyl-L-alanyl-L-asparaginyl-L-phenylalanyl-L-leucyl-L-valyl-L-histidyl-L-seryl-L-seryl-L-asparaginyl-L-asparaginyl-L-phenylalanylglycyl-L-prolyl-L-isoleucyl-L-leucyl-L-prolyl-L-prolyl-L-threonyl-L-asparaginyl-L-valylglycyl-L-seryl-L-asparaginyl-L-threonyl- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 14: PN: US20050143303 SEQID: 14 claimed protein
CI MAN
SQL 37

SEQ 1 KCNTATCATQ RLANFLVHSS NNFGPILPPT NVGSNTY
========== ========== ========== =======
HITS AT: 1-37

RELATED SEQUENCES AVAILABLE WITH SEQLINK

REFERENCE 1: 143:103229

L1 ANSWER 3 OF 14 REGISTRY COPYRIGHT 2006 ACS on STN
RN 562138-05-0 REGISTRY
CN L-Tyrosine, L-lysyl-L-cysteinyl-L-asparaginyl-L-threonyl-L-alanyl-L-threonyl-L-cysteinyl-L-alanyl-L-threonyl-L-glutaminyl-L-arginyl-L-leucyl-L-alanyl-L-asparaginyl-L-phenylalanyl-L-leucyl-L-valyl-L-histidyl-L-seryl-L-seryl-L-asparaginyl-L-asparaginyl-L-phenylalanylglycyl-L-prolyl-L-isoleucyl-L-leucyl-L-prolyl-L-prolyl-L-threonyl-L-asparaginyl-L-valylglycyl-L-seryl-L-asparaginyl-L-threonyl- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 2138: PN: WO03060071 SEQID: 2200 unclaimed protein
CI MAN
SQL 37

SEQ 1 KCNTATCATQ RLANFLVHSS NNFGPILPPT NVGSNTY
========== ========== ========== =======
HITS AT: 1-37

RELATED SEQUENCES AVAILABLE WITH SEQLINK

REFERENCE 1: 139:122690

L1 ANSWER 4 OF 14 REGISTRY COPYRIGHT 2006 ACS on STN
RN 538377-77-4 REGISTRY
CN L-Tyrosinamide, L-lysyl-L-cysteinyl-L-asparaginyl-L-threonyl-L-alanyl-L-threonyl-L-cysteinyl-L-alanyl-L-threonyl-L-glutaminyl-L-arginyl-L-leucyl-L-alanyl-L-asparaginyl-L-phenylalanyl-L-leucyl-L-valyl-L-histidyl-L-seryl-L-seryl-L-asparaginyl-L-asparaginyl-L-phenylalanylglycyl-L-prolyl-L-isoleucyl-L-leucyl-L-prolyl-L-prolyl-L-threonyl-L-asparaginyl-L-valylglycyl-L-seryl-L-asparaginyl-L-threonyl-, cyclic (2→7)-disulfide (9CI) (CA INDEX NAME)
CI MAN
SQL 37

SEQ 1 KCNTATCATQ RLANFLVHSS NNFGPILPPT NVGSNTY
========== ========== ========== =======

HITS AT: 1-37

RELATED SEQUENCES AVAILABLE WITH SEQLINK

REFERENCE 1: 139:17664

L1 ANSWER 5 OF 14 REGISTRY COPYRIGHT 2006 ACS on STN
RN 294869-29-7 REGISTRY
CN L-Tyrosinamide, L-lysyl-D-cysteinyl-L-asparaginyl-L-threonyl-L-alanyl-L-threonyl-L-cysteinyl-L-alanyl-L-threonyl-L-glutaminyl-L-arginyl-L-leucyl-L-alanyl-L-asparaginyl-L-phenylalanyl-L-leucyl-L-valyl-L-histidyl-L-seryl-L-seryl-L-asparaginyl-L-asparaginyl-L-phenylalanylglycyl-L-prolyl-L-isoleucyl-L-leucyl-L-prolyl-L-prolyl-L-threonyl-L-asparaginyl-L-valylglycyl-L-seryl-L-asparaginyl-L-threonyl-, cyclic (2→7)-disulfide (9CI) (CA INDEX NAME)
CI MAN
SQL 37

SEQ 1 KCNTATCATQ RLANFLVHSS NNFGPILPPT NVGSNTY
========== ========== ========== =======
HITS AT: 1-37

RELATED SEQUENCES AVAILABLE WITH SEQLINK

REFERENCE 1: 133:256877

L1 ANSWER 6 OF 14 REGISTRY COPYRIGHT 2006 ACS on STN
RN 294869-28-6 REGISTRY
CN L-Tyrosinamide, D-lysyl-L-cysteinyl-L-asparaginyl-L-threonyl-L-alanyl-L-threonyl-L-cysteinyl-L-alanyl-L-threonyl-L-glutaminyl-L-arginyl-L-leucyl-L-alanyl-L-asparaginyl-L-phenylalanyl-L-leucyl-L-valyl-L-histidyl-L-seryl-L-seryl-L-asparaginyl-L-asparaginyl-L-phenylalanylglycyl-L-prolyl-L-isoleucyl-L-leucyl-L-prolyl-L-prolyl-L-threonyl-L-asparaginyl-L-valylglycyl-L-seryl-L-asparaginyl-L-threonyl-, cyclic (2→7)-disulfide (9CI) (CA INDEX NAME)
CI MAN
SQL 37

SEQ 1 KCNTATCATQ RLANFLVHSS NNFGPILPPT NVGSNTY
========== ========== ========== =======
HITS AT: 1-37

RELATED SEQUENCES AVAILABLE WITH SEQLINK

REFERENCE 1: 133:256877

L1 ANSWER 7 OF 14 REGISTRY COPYRIGHT 2006 ACS on STN
RN 294869-27-5 REGISTRY
CN D-Tyrosinamide, L-lysyl-L-cysteinyl-L-asparaginyl-L-threonyl-L-alanyl-L-threonyl-L-cysteinyl-L-alanyl-L-threonyl-L-glutaminyl-L-arginyl-L-leucyl-L-alanyl-L-asparaginyl-L-phenylalanyl-L-leucyl-L-valyl-L-histidyl-L-seryl-L-seryl-L-asparaginyl-L-asparaginyl-L-phenylalanylglycyl-L-prolyl-L-isoleucyl-L-leucyl-L-prolyl-L-prolyl-L-threonyl-L-asparaginyl-L-valylglycyl-L-seryl-L-asparaginyl-L-threonyl-, cyclic (2→7)-disulfide (9CI) (CA INDEX NAME)
CI MAN
SQL 37

SEQ 1 KCNTATCATQ RLANFLVHSS NNFGPILPPT NVGSNTY
========== ========== ========== =======

HITS AT: 1-37

RELATED SEQUENCES AVAILABLE WITH SEQLINK

REFERENCE 1: 133:256877

L1 ANSWER 8 OF 14 REGISTRY COPYRIGHT 2006 ACS on STN
RN 294869-26-4 REGISTRY
CN L-Tyrosinamide, L-lysyl-L-cysteinyl-L-asparaginyl-L-threonyl-D-alanyl-L-threonyl-L-cysteinyl-L-alanyl-L-threonyl-L-glutaminyl-L-arginyl-L-leucyl-L-alanyl-L-asparaginyl-L-phenylalanyl-L-leucyl-L-valyl-L-histidyl-L-seryl-L-seryl-L-asparaginyl-L-asparaginyl-L-phenylalanylglycyl-L-prolyl-L-isoleucyl-L-leucyl-L-prolyl-L-prolyl-L-threonyl-L-asparaginyl-L-valylglycyl-L-seryl-L-asparaginyl-L-threonyl-, cyclic (2→7)-disulfide (9CI) (CA INDEX NAME)
CI MAN
SQL 37

SEQ 1 KCNTATCATQ RLANFLVHSS NNFGPILPPT NVGSNTY
========== ========== ========== =======
HITS AT: 1-37

RELATED SEQUENCES AVAILABLE WITH SEQLINK

REFERENCE 1: 133:256877

L1 ANSWER 9 OF 14 REGISTRY COPYRIGHT 2006 ACS on STN
RN 294869-25-3 REGISTRY
CN L-Tyrosinamide, L-lysyl-L-cysteinyl-L-asparaginyl-L-threonyl-L-alanyl-L-threonyl-L-cysteinyl-D-alanyl-L-threonyl-L-glutaminyl-L-arginyl-L-leucyl-L-alanyl-L-asparaginyl-L-phenylalanyl-L-leucyl-L-valyl-L-histidyl-L-seryl-L-seryl-L-asparaginyl-L-asparaginyl-L-phenylalanylglycyl-L-prolyl-L-isoleucyl-L-leucyl-L-prolyl-L-prolyl-L-threonyl-L-asparaginyl-L-valylglycyl-L-seryl-L-asparaginyl-L-threonyl-, cyclic (2→7)-disulfide (9CI) (CA INDEX NAME)
CI MAN
SQL 37

SEQ 1 KCNTATCATQ RLANFLVHSS NNFGPILPPT NVGSNTY
========== ========== ========== =======
HITS AT: 1-37

RELATED SEQUENCES AVAILABLE WITH SEQLINK

REFERENCE 1: 133:256877

L1 ANSWER 10 OF 14 REGISTRY COPYRIGHT 2006 ACS on STN
RN 294869-17-3 REGISTRY
CN L-Tyrosinamide, L-lysyl-L-cysteinyl-L-asparaginyl-L-threonyl-D-alanyl-L-threonyl-L-cysteinyl-D-alanyl-L-threonyl-L-glutaminyl-L-arginyl-L-leucyl-L-alanyl-L-asparaginyl-L-phenylalanyl-L-leucyl-L-valyl-L-histidyl-L-seryl-L-seryl-L-asparaginyl-L-asparaginyl-L-phenylalanylglycyl-L-prolyl-L-isoleucyl-L-leucyl-L-prolyl-L-prolyl-L-threonyl-L-asparaginyl-L-valylglycyl-L-seryl-L-asparaginyl-L-threonyl-, cyclic (2→7)-disulfide (9CI) (CA INDEX NAME)
CI MAN
SQL 37

SEQ 1 KCNTATCATQ RLANFLVHSS NNFGPILPPT NVGSNTY
========== ========== ========== =======

HITS AT: 1-37

RELATED SEQUENCES AVAILABLE WITH SEQLINK

REFERENCE 1: 133:256877

L1 ANSWER 11 OF 14 REGISTRY COPYRIGHT 2006 ACS on STN
RN 294869-16-2 REGISTRY
CN L-Tyrosinamide, L-lysyl-L-cysteinyl-L-asparaginyl-L-threonyl-L-alanyl-L-threonyl-L-cysteinyl-L-alanyl-L-threonyl-L-glutaminyl-L-arginyl-D-leucyl-L-alanyl-L-asparaginyl-L-phenylalanyl-L-leucyl-L-valyl-L-histidyl-L-seryl-L-seryl-L-asparaginyl-L-asparaginyl-L-phenylalanylglycyl-L-prolyl-L-isoleucyl-L-leucyl-L-prolyl-L-prolyl-L-threonyl-L-asparaginyl-L-valylglycyl-L-seryl-L-asparaginyl-L-threonyl-, cyclic (2→7)-disulfide (9CI) (CA INDEX NAME)
CI MAN
SQL 37

SEQ 1 KCNTATCATQ RLANFLVHSS NNFGPILPPT NVGSNTY
========== ========== ========== =======
HITS AT: 1-37

RELATED SEQUENCES AVAILABLE WITH SEQLINK

REFERENCE 1: 133:256877

L1 ANSWER 12 OF 14 REGISTRY COPYRIGHT 2006 ACS on STN
RN 187887-46-3 REGISTRY
CN Amylin (human), 25-L-proline-28-L-proline-29-L-proline-, acetate (salt) (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN L-Tyrosinamide, L-lysyl-L-cysteinyl-L-asparaginyl-L-threonyl-L-alanyl-L-threonyl-L-cysteinyl-L-alanyl-L-threonyl-L-glutaminyl-L-arginyl-L-leucyl-L-alanyl-L-asparaginyl-L-phenylalanyl-L-leucyl-L-valyl-L-histidyl-L-seryl-L-seryl-L-asparaginyl-L-asparaginyl-L-phenylalanylglycyl-L-prolyl-L-isoleucyl-L-leucyl-L-prolyl-L-prolyl-L-threonyl-L-asparaginyl-L-valylglycyl-L-seryl-L-asparaginyl-L-threonyl-, cyclic (2→7)-disulfide, acetate (salt)
OTHER NAMES:
CN AC 0137
CN Pramlintide acetate
CN Symlin
CI COM
SQL 37

SEQ 1 KCNTATCATQ RLANFLVHSS NNFGPILPPT NVGSNTY
========== ========== ========== =======
HITS AT: 1-37

RELATED SEQUENCES AVAILABLE WITH SEQLINK

REFERENCE 1: 144:286193

REFERENCE 2: 144:285389

REFERENCE 3: 143:260439

REFERENCE 4: 143:91290

REFERENCE 5: 142:457348

REFERENCE 6: 140:199313

REFERENCE 7: 137:242215

REFERENCE 8: 136:95388

REFERENCE 9: 135:298797

REFERENCE 10: 135:272869

L1 ANSWER 13 OF 14 REGISTRY COPYRIGHT 2006 ACS on STN
RN 153190-93-3 REGISTRY
CN L-Tyrosine, L-lysyl-L-cysteinyl-L-asparaginyl-L-threonyl-L-alanyl-L-threonyl-L-cysteinyl-L-alanyl-L-threonyl-L-glutaminyl-L-arginyl-L-leucyl-L-alanyl-L-asparaginyl-L-phenylalanyl-L-leucyl-L-valyl-L-histidyl-L-seryl-L-seryl-L-asparaginyl-L-asparaginyl-L-phenylalanylglycyl-L-prolyl-L-isoleucyl-L-leucyl-L-prolyl-L-prolyl-L-threonyl-L-asparaginyl-L-valylglycyl-L-seryl-L-asparaginyl-L-threonyl-, cyclic (2→7)-disulfide (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 1,2-Dithia-5,8,11,14,17-pentaazacycloeicosane, cyclic peptide deriv.
CI MAN
SQL 37

SEQ 1 KCNTATCATQ RLANFLVHSS NNFGPILPPT NVGSNTY
========== ========== ========== =======
HITS AT: 1-37

RELATED SEQUENCES AVAILABLE WITH SEQLINK

REFERENCE 1: 133:256877

REFERENCE 2: 131:262707

REFERENCE 3: 129:45364

REFERENCE 4: 120:129053

L1 ANSWER 14 OF 14 REGISTRY COPYRIGHT 2006 ACS on STN
RN 151126-32-8 REGISTRY
CN Amylin (human), 25-L-proline-28-L-proline-29-L-proline- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN 1,2-Dithia-5,8,11,14,17-pentaazacycloeicosane, cyclic peptide deriv.
CN L-Tyrosinamide, L-lysyl-L-cysteinyl-L-asparaginyl-L-threonyl-L-alanyl-L-threonyl-L-cysteinyl-L-alanyl-L-threonyl-L-glutaminyl-L-arginyl-L-leucyl-L-alanyl-L-asparaginyl-L-phenylalanyl-L-leucyl-L-valyl-L-histidyl-L-seryl-L-seryl-L-asparaginyl-L-asparaginyl-L-phenylalanylglycyl-L-prolyl-L-isoleucyl-L-leucyl-L-prolyl-L-prolyl-L-threonyl-L-asparaginyl-L-valylglycyl-L-seryl-L-asparaginyl-L-threonyl-, cyclic (2→7)-disulfide
OTHER NAMES:
CN Pramlintide
CN Triproamylin
CI COM, MAN
SQL 37

SEQ 1 KCNTATCATQ RLANFLVHSS NNFGPILPPT NVGSNTY
========== ========== ========== =======

HITS AT: 1-37

RELATED SEQUENCES AVAILABLE WITH SEQLINK

REFERENCE 1: 144:370423

REFERENCE 2: 144:285403

REFERENCE 3: 144:254119

REFERENCE 4: 144:204886

REFERENCE 5: 144:64561

REFERENCE 6: 143:398577

REFERENCE 7: 143:319551

REFERENCE 8: 143:279778

REFERENCE 9: 143:242382

REFERENCE 10: 143:228799

FILE 'CAPLUS' ENTERED AT 12:08:27 ON 16 MAY 2006
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FILE COVERS 1907 - 16 May 2006 VOL 144 ISS 21
FILE LAST UPDATED: 15 May 2006 (20060515/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply. They are available for your review at:

http://www.cas.org/infopolicy.html

L2 111 SEA ABB=ON PLU=ON L1
L3 35 SEA ABB=ON PLU=ON L2 AND (ANTIOBES? OR OBESE OR OBESITY OR (WEIGH? OR WT)(3A)GAIN? OR APPETITE(3A)(DEPRESS? OR SUPPRESS?) OR ((BODY OR BODILY)(W)(WT OR WEIGH?))(3A)REDUC?)

L3 ANSWER 1 OF 35 CAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 21 Apr 2006
ACCESSION NUMBER: 2006:367143 CAPLUS
TITLE: Rhodanine derivatives as PPAR receptor modulators and their preparation, pharmaceutical compositions and use for treatment and prophylaxis of various

diseases

INVENTOR(S): Sarshar, Sepehr; Marappan, Subrumanian
PATENT ASSIGNEE(S): Auspex Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 106 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

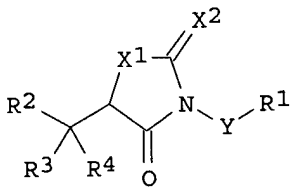
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006041921	A2	20060420	WO 2005-US35832	20051004

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW

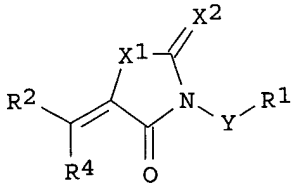
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2004-616574P P 20041005

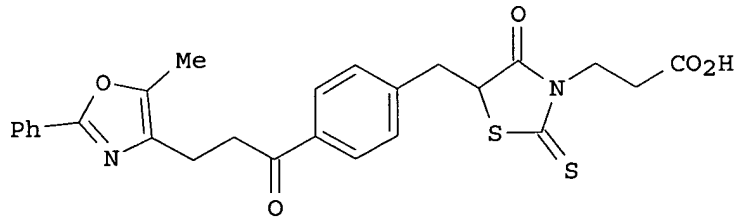
GI



I



II



III

AB Processes for the preparation of compds. of formulas I and II are described. These compds. can be used as PPAR modulators and for the treatment and/or management of cancer, inflammation, cellular differentiation and proliferation, wound healing, metabolism of lipids and carbohydrates, **obesity**, diabetes, and energy homeostasis. Compds. of formula I and II wherein X1 and X2 are independently O, S, or NH; Y is (un)substituted C1-10 alkyl; R1 is (un)substituted C5-11

oxocycloalkenyl, (R9CO)(R10CO)CH, or (un)substituted dioxodioxanyl; R9 and R10 are independently OH, alkoxyl, aryloxy, NH2, alkylamino, arylamino, N-aryl-N-alkylamino, -NHNH2, alkylhydrazino, arylhydrazino, N-aryl-N-alkylamino, NHOH and derivs., alkyl, or aryl; R2 and R3 are independently H, halo, or alkyl; R4 is substituted aryl and heteroaryl; and their pharmaceutically acceptable salts, and prodrugs thereof are claimed. Example compound III was prepared by addition of methyllithium to 4-(diethoxymethyl)benzaldehyde to give the corresponding alc., which was oxidized to give 4-(diethoxymethyl)acetophenone, which underwent acylation with di-Et carbonate; the resulting 2-[4-(diethoxymethyl)benzoyl]acetate underwent alkylation with 4-chloromethyl-5-methyl-2-phenyloxazole followed by decarboxylation to give 4-[3-(5-methyl-2-phenyl-4-oxazolyl)propionyl]benzaldehyde, which underwent condensation with rhodanine-N-propionic acid to give 4-[3-(5-methyl-2-phenyl-4-oxazolyl)propionyl]benzylidene-3-(β-carboxyethyl)rhodanine, which underwent hydrogenation to give example compound III. The invention compds. were evaluated for their PPAR-γ modulating activity. From the assay, it was determined example compound III exhibited an EC50 0.127 μM.

IT **187887-46-3**, Symlin
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preparation of rhodanine derivs. as PPAR receptors modulators useful in treatment and prophylaxis of diseases)

L3 ANSWER 2 OF 35 CAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 16 Mar 2006
ACCESSION NUMBER: 2006:232071 CAPLUS
DOCUMENT NUMBER: 144:286193
TITLE: Treating **obesity** with combination therapeutics comprising ciliary neurotrophic factor
INVENTOR(S): Yancopoulos, George D.; Wiegand, Stanley J.; Sleeman, Mark W.; Koehler-Stec, Ellen-Marie
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 12 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2006058224	A1	20060316	US 2005-229426	20050915
WO 2006032042	A2	20060323	WO 2005-US33313	20050915

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

PRIORITY APPLN. INFO.: US 2004-609926P P 20040915

AB The present invention relates to compns. and methods of treating **obesity** or **obesity**-related condition, including **reducing body-weight**, improving-diabetic parameters, metabolic syndrome. liver steatosis, and/or hypertension with a combination of CNTF or a CNTF-related mol. and a second agent which is a therapeutic mol. useful in the treatment of **obesity**, type II diabetes, or other **obesity**-related conditions. Ciliary neurotrophic factor (CNTF) is a protein that is required for the survival of embryonic chick ciliary ganglion neurons in vitro (Manthorpe et al., 1980, J. Neurochem. 34:69-75). The invention is based in part on observation that administration of the modified CNTF mol. Axokine.TM. in combination with a second agent results in a far greater improvement in body weight and diabetic parameters such as fasting glucose and insulin levels, oral glucose tolerance, triglycerides and nonesterified free-fatty acids than can be achieved by comparable food restriction or with either agent alone.

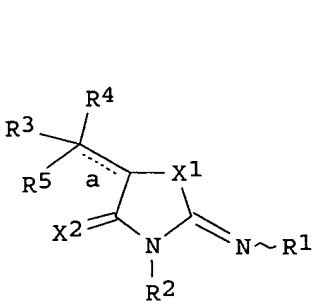
IT **187887-46-3**, Symlin
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination therapy with CNTF; treating **obesity** with combination therapeutics comprising ciliary neurotrophic factor)

L3 ANSWER 3 OF 35 CAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 23 Feb 2006
ACCESSION NUMBER: 2006:167017 CAPLUS
DOCUMENT NUMBER: 144:254119
TITLE: Preparation of thiazolidinones and related heterocyclic compounds as farnesoid X receptor agonists with therapeutic uses
INVENTOR(S): Martin, Richard; Flatt, Brenton Todd; Kahl, Jeffrey Dean
PATENT ASSIGNEE(S): Exelixis, Inc., USA
SOURCE: PCT Int. Appl., 146 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

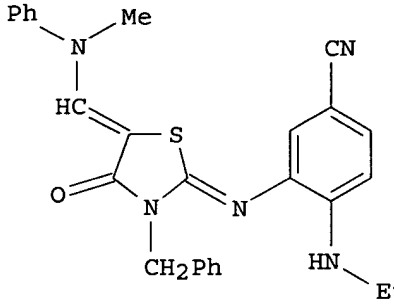
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2006020680	A2	20060223	WO 2005-US28357	20050809
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				

PRIORITY APPLN. INFO.: US 2004-600239P P 20040810

OTHER SOURCE(S): MARPAT 144:254119
GI



I



II

AB Thiazolidinones and related heterocyclic compds. (shown as I; variables defined below; e.g. 3-[[3-benzyl-5-[[N-methyl-N-(phenyl)amino]methylene]-4-oxothiazolidin-2-ylidene]amino]-4-ethylaminobenzonitrile (shown as II)), compns. and methods for modulating the activity of receptors are provided. In particular, compds. and compns. are provided for modulating the activity of receptors and for the treatment, prevention, or amelioration of ≥1 symptoms of the disease or disorder directly or indirectly related to the activity of the receptors. For I: bond a is a single or double bond; X1 is NR6, O or S(O)t (t = 0-2); X2 is S or O; R1 is (un)substituted alkyl, alkenyl or alkynyl; or R1 is (un)substituted cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, aryl, aralkyl, heteroaryl or heteroaralkyl; or R1 is -R9N(R11)(R12), -R9C(J)R13, -R9C(J)OR10, -R9C(J)N(R11)(R12), -R9N(R10)C(J)R13, -R9N(R10)C(J)OR10, -R9S(O)tR15 or -R9N(R10)C(J)N(R11)(R12). R2 is (un)substituted alkyl, alkenyl, alkynyl; or R2 is (un)substituted cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, aryl, heteroaryl, aralkyl, heteroaralkyl or aryl; or R2 is -R9C(J)R13, -R9C(J)OR10, -R9C(J)N(R11)(R12), -R9C(J)N(R10)N(R11)(R12), -R9N(R10)C(J)R13, -R9N(R10)C(J)OR10, -R9N(R10)C(J)N(R11)(R12), -R9N(R11)(R12) or -R9S(O)tR15; R3, R4 and R5 = (un)substituted alkyl, alkenyl or alkynyl; or R3, R4 and R5 = (un)substituted cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, aryl, aralkyl, heteroaryl, or heteroaralkyl; or R3, R4 and R5 = H, halo, -N(R7)(R8), -N(R10)C(J)R13, -N(R10)C(J)OR10, -R9C(J)R13, -N(R10)C(J)N(R11)(R12) and -N(R10)S(O)tR15; each J = O or S; addnl. details including provisos are given in the claims. Although the methods of preparation are not claimed, prepns. and/or characterization data for >10 examples of I are included. For example, II was prepared in 5 steps (82, 100, 93, 87, 58, resp.) starting with substitution of 4-fluoro-3-nitrobenzonitrile by ethylamine to give 4-ethylamino-3-nitrobenzonitrile, which was reduced to 3-amino-4-ethylaminobenzonitrile, which was added to benzyl isothiocyanate to give 1-benzyl-3-(5-cyano-2-ethylaminophenyl)thiourea, which was cyclocondensed with Et chloroacetate to give 3-[(3-benzyl-4-oxothiazolidin-2-ylidene)amino]-4-ethylaminobenzonitrile, which was condensed with tri-Me orthoformate and N-methylaniline to give II.

IT **151126-32-8**, Pramlintide
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; preparation of thiazolidinones and related heterocyclic compds. as farnesoid X receptor agonists with therapeutic uses)

L3 ANSWER 4 OF 35 CAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 10 Nov 2005
ACCESSION NUMBER: 2005:1195074 CAPLUS
DOCUMENT NUMBER: 144:204886

TITLE: Drugs on the horizon for diabesity
AUTHOR(S): Bailey, Clifford J.
CORPORATE SOURCE: Diabetes Group, Life and Health Sciences, Aston University, Birmingham, B4 7ET, UK
SOURCE: Current Diabetes Reports (2005), 5(5), 353-359
CODEN: CDRUAK; ISSN: 1534-4827
PUBLISHER: Current Science Inc.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. The coexistence of type 2 diabetes and **obesity** presents a complex therapeutic challenge. Future combination tablets may include agents to address diabetes and any accompanying cardiovascular risk factors. Injectable agents that improve glycemic control and facilitate weight loss have recently become available: the soluble amylin analog pramlintide provides an adjunct to insulin therapy in type 1 and type 2 diabetes, and the incretin mimetic exenatide can enhance prandial insulin release in type 2 diabetes. Orally active inhibitors of the incretin-degrading enzyme dipeptidyl peptidase-IV, agonists of peroxisome proliferator-activated receptor (PPAR)-α and PPAR-γ ("dual PPARs"), and the CBI cannabinoid receptor inhibitor rimonabant are advanced in clin. development. Many novel antidiabetic and **antiobesity** compds. are emerging in preclin. development.

IT **151126-32-8**, Pramlintide
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(developing amylin analog pramlintide can address different facet of disease and can be part of intensive and inclusive strategy to prevent associated vascular complication in type 2 diabetes patient)

REFERENCE COUNT: 72 THERE ARE 72 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 5 OF 35 CAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 09 Sep 2005
ACCESSION NUMBER: 2005:985311 CAPLUS
DOCUMENT NUMBER: 143:279778
TITLE: Methods for affecting body composition using amylin or amylin analogs
INVENTOR(S): Mack, Christine Marie; Roth, Jonathan David
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 41 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005197287	A1	20050908	US 2004-851574	20040520
WO 2005115437	A2	20051208	WO 2005-US17227	20050517

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW,

AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2004-550447P P 20040304
US 2004-851574 A 20040520

AB Methods for affecting body composition include the use of amylin or amylin agonist(s). Total **body weight** may be **reduced**, maintained or even increased; however, the body fat is reduced or body fat gain is prevented, while lean body mass is maintained or increased.

IT **151126-32-8P**
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(methods for affecting body composition using amylin or amylin analogs)

L3 ANSWER 6 OF 35 CAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 26 Aug 2005
ACCESSION NUMBER: 2005:902741 CAPLUS
DOCUMENT NUMBER: 143:242382
TITLE: Hybrid polypeptides with selectable properties for treatment of metabolic diseases and disorders
INVENTOR(S): Levy, Odile Esther; Hanley, Michael R.; Jodka, Carolyn M.; Lewis, Diana Y.; Soares, Christopher J.; Ghosh, Soumitra S.; D'Souza, Lawrence J.; Parkes, David G.; Mack, Christine M.
PATENT ASSIGNEE(S): Amylin Pharmaceuticals, Inc., USA
SOURCE: 113 pp.
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005077072	A2	20050825	WO 2005-US4178	20050211
WO 2005077072	A3	20060302		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, SM				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2006094652	A1	20060504	US 2005-55093	20050211

PRIORITY APPLN. INFO.: US 2004-543407P P 20040211

AB The present invention relates generally to novel, selectable hybrid polypeptides useful as agents for the treatment and prevention of metabolic diseases and disorders which can be alleviated by control plasma glucose levels, insulin levels, and/or insulin secretion, such as diabetes and diabetes-related conditions. Such conditions and

disorders include, but are not limited to, hypertension, dyslipidemia, cardiovascular disease, eating disorders, insulin-resistance, **obesity**, and diabetes mellitus of any kind, including type 1, type 2, and gestational diabetes. The hybrid polypeptides of the invention comprise at least two bioactive peptide hormone modules covalently linked together, wherein at least one of the bioactive peptide hormone modules exhibits at least one hormonal activity of a component peptide hormone. The bioactive peptide hormone modules are independently selected from: component peptide hormones; fragments, analogs and derivs. of the component peptide hormones; and peptidic enhancers.

IT **151126-32-8D**, hybrid polypeptides
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(hybrid polypeptides with selectable properties for treatment of metabolic diseases and disorders)

L3 ANSWER 7 OF 35 CAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 29 Jul 2005
ACCESSION NUMBER: 2005:669282 CAPLUS
DOCUMENT NUMBER: 143:260439
TITLE: Amylin analogue as an antidiabetic agent
AUTHOR(S): Day, Caroline
CORPORATE SOURCE: Diabetes Group, Life and Health Sciences, Aston University, Birmingham, B4 7ET, UK
SOURCE: British Journal of Diabetes & Vascular Disease (2005), 5(3), 151-154
CODEN: BJDVAI; ISSN: 1474-6514
PUBLISHER: MediNews (Diabetes) Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. The amylin analog pramlintide (SYMLIN) is the first in a new class of injectable amylinomimetic agents to be approved for the treatment of diabetes. This adjunct to insulin treatment of type 1 and type 2 diabetes has recently been approved for use in the USA. Pramlintide, unlike native amylin is soluble It acts mainly via central effects (Area postrema) resulting in deceased glucagon secretion, slowing gastric emptying and a satiety effect. It is injected s.c. sep. from insulin, and usually before each of the main meals. It has been shown to improve glycemic control without causing **weight gain** but the dose must be titrated slowly in association with appropriate insulin adjustments to guard against insulin-induced hypoglycemia and nausea. Thus, pramlintide is an injected amylin replacement therapy that can be used with an insulin regimen to improve glycemic control without **weight gain.**

IT **187887-46-3**, SYMLIN
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pramlintide; amylin analog as antidiabetic agent)

REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 8 OF 35 CAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 06 Jul 2005
ACCESSION NUMBER: 2005:580674 CAPLUS
DOCUMENT NUMBER: 143:398577
TITLE: Emerging therapies: going beyond insulin in treating individuals with type 1 diabetes mellitus
AUTHOR(S): Allard, Felicia D.; Wallace, Amy E.; Greenbaum,

Carla J.
CORPORATE SOURCE: Barbara Davis Center for Childhood Diabetes, University of Colorado Health Sciences Center, Denver, CO, USA
SOURCE: Current Opinion in Endocrinology & Diabetes (2005), 12(4), 303-308
CODEN: CENDES; ISSN: 1068-3097
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB Purpose of review: New therapeutic options for individuals with type 1 diabetes mellitus are emerging. This review discusses novel noninsulin therapeutics that are in clin. trials or have recently been approved. Recent findings: Amylin is cosecreted with insulin in β cells, and thus, like insulin, is absent in individuals with long-standing type 1 diabetes mellitus. Synthetic amylin or pramlintide is a preprandial injectable drug that suppresses post-prandial hyperglycemia and has mild effects on glycosylated Hb with either no change or a **reduction** in **body weight** Several incretin mimetics in clin. development are likely to have similar therapeutic effects. Exciting preclin. data with these agents as well as other growth factors suggest that they may encourage islet neogenesis while suppressing apoptosis. Although there are as yet no clin. data supporting such tantalizing effects on β-cell mass, clin. trials in various populations are planned or underway. Summary: Novel noninsulin agents are beginning to expand the armamentarium of clinicians treating patients with type 1 diabetes mellitus.

IT **151126-32-8**, Pramlintide
RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(synthetic pramlintide control post-prandial hyperglycemia, increase islet cell neogenesis and reduce apoptosis in type I diabetes mellitus patient)

REFERENCE COUNT: 63 THERE ARE 63 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 9 OF 35 CAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 01 Jul 2005
ACCESSION NUMBER: 2005:572578 CAPLUS
DOCUMENT NUMBER: 143:103229
TITLE: Intranasal administration of glucose-regulating peptides
INVENTOR(S): Quay, Steven C.; Costantino, Henry R.
PATENT ASSIGNEE(S): Nastech Pharmaceutical Company Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 55 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005143303	A1	20050630	US 2004-991597	20041118
WO 2005065714	A1	20050721	WO 2004-US43312	20041217

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP,

KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW,
MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD,
SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ,
VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW,
AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ,
DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC,
NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA,
GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2006074025	A1	20060406	US 2005-293676	20051202
PRIORITY APPLN. INFO.:			US 2003-532337P	P 20031226
			US 2004-991597	A2 20041118

AB Pharmaceutical compns. and methods are described comprising at least one glucose-regulating peptide, such as amylin, glucagon-like peptide-1 (GLP), pramlintide or exendin-4 and one or more mucosal delivery-enhancing agents for enhanced nasal mucosal delivery of the amylin, for treating a variety of diseases and conditions in mammalian subjects, including **obesity** and diabetes mellitus. A formulation contained anhydrous chlorobutanol 0.50, Me β-cyclodextrin 4.5, didecanoyl L-α-phospahtidylcholine 0.1, disodium edetate 0.1, sodium citrate dihydrate 0.162, citric acid 0.086, α-lactose monohydrate 0.9, sorbitol 1.82, exendin-4 0.1, and water qs to 100%.

IT **151126-32-8**, Pramlintide **856043-00-0**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(intranasal administration of glucose-regulating peptides)

L3 ANSWER 10 OF 35 CAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 30 May 2005

ACCESSION NUMBER:	2005:455805 CAPLUS
DOCUMENT NUMBER:	143:1522
TITLE:	Adjunctive therapy with pramlintide lowers HbA1c without concomitant **weight gain** and increased risk of severe hypoglycemia in patients with type 1 diabetes approaching glycemic targets
AUTHOR(S):	Ratner, R.; Whitehouse, F.; Fineman, M. S.; Strobel, S.; Shen, L.; Maggs, D. G.; Kolterman, O. G.; Weyer, C.
CORPORATE SOURCE:	MedStar Clinical Research Institute, Washington, DC, USA
SOURCE:	Experimental and Clinical Endocrinology & Diabetes (2005), 113(4), 199-204 CODEN: ECEDFQ; ISSN: 0947-7349
PUBLISHER:	J. A. Barth Verlag
DOCUMENT TYPE:	Journal
LANGUAGE:	English

AB In long-term clin. trials in patients with type 1 diabetes spanning a wide range of HbA1c, addition of pramlintide to existing insulin regimens led to redns. in HbA1c that were accompanied by weight loss and no increase in overall severe hypoglycemia event rates. Given that **weight gain** and increased hypoglycemia risk contribute to the difficulty of attaining HbA1c targets (< 7%), the question arose whether pramlintide could benefit patients approaching, but not reaching glycemic targets with insulin alone. To address this question, we conducted a pooled anal. from 3 long-term clin. trials, including all patients with an entry HbA1c between 7.0% and 8.5%. Within the subset of patients with an entry HbA1c between 7.0% and

8.5% (approx. 28% of all patients enrolled in the 3 studies), 196 were treated with placebo + insulin (baseline HbA1c 7.9±0.4%, body weight 76.0±14.3 kg [mean ± SD]) and 281 with pramlintide + insulin (baseline HbA1c 7.9±0.4%, body weight 75.4±13.1 kg). Endpoints included placebo-corrected changes from baseline to week 26 in HbA1c, body weight, and the event rate of severe hypoglycemia. Adjunctive therapy with pramlintide resulted in significant **redns.** in HbA1c and **body weight** from baseline to week 26 (0.3% and 1.8 kg, placebo-corrected treatment differences, resp., both $p \leq 0.0009$). These changes occurred without an increase in the overall risk of severe hypoglycemia (1.40 pramlintide vs. 1.86 placebo, events/patient-year of exposure). Addition of pramlintide to insulin therapy may help patients with type 1 diabetes who are approaching, but not yet reaching, glycemic targets with insulin alone to achieve further redns. in HbA1c without concomitant **weight gain** and increased risk of severe hypoglycemia.

IT **151126-32-8**, Pramlintide
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pramlintide addition to insulin lowers HbA1c without **weight gain** or increased hypoglycemia in IDDM patients)

REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 11 OF 35 CAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 17 May 2005
ACCESSION NUMBER: 2005:418272 CAPLUS
DOCUMENT NUMBER: 143:228799
TITLE: Effect of pramlintide on satiety and food intake in **obese** subjects and subjects with type 2 diabetes
AUTHOR(S): Chapman, I.; Parker, B.; Doran, S.; Feinle-Bisset, C.; Wishart, J.; Strobel, S.; Wang, Y.; Burns, C.; Lush, C.; Weyer, C.; Horowitz, M.
CORPORATE SOURCE: Department of Medicine, Royal Adelaide Hospital, University of Adelaide, Adelaide, South Australia, Australia
SOURCE: Diabetologia (2005), 48(5), 838-848
CODEN: DBTGAJ; ISSN: 0012-186X
PUBLISHER: Springer GmbH
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Long-term trials in insulin-treated subjects with type 2 diabetes have shown that adjunctive treatment with the amylin analog pramlintide reduces HbA1c levels and elicits weight loss. While amylin reduces food intake in rodents, pramlintide's effect on satiety and food intake in humans has not yet been assessed. In this randomized, double-blind, placebo-controlled crossover study, 11 insulin-treated men with type 2 diabetes (age 60±9 years, BMI 28.9±4.8 kg/m2) and 15 non-diabetic **obese** men (age 41±21 years, BMI 34.4±4.5 kg/m2) underwent 2 standardized meal tests. After fasting overnight, subjects received single s.c. injections of either pramlintide (120 μg) or placebo, followed by a preload meal. After 1 h, subjects ate an ad libitum buffet meal. Energy intake and meal duration were measured, as were hunger ratings (using visual analog scales), and plasma cholecystokinin, glucagon-like peptide-1 and peptide YY concns. over time. Compared with placebo, pramlintide reduced energy intake in both the type 2 diabetes (Δ-202±64 kcal, -23±8%, $p<0.01$) and **obese** (Δ-170±68 kcal, -16±6%,

p<0.02) groups, without affecting meal duration. Hunger and hormonal analyte profiles provided evidence that pramlintide may exert a primary satiogenic effect, independently of other anorexigenic gut peptides. The results indicate that enhanced satiety and reduced food intake may explain the weight loss observed in long-term pramlintide trials.

IT **151126-32-8**, Pramlintide
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(effect of pramlintide on satiety and food intake in **obese** subjects and subjects with type 2 diabetes)

REFERENCE COUNT: 49 THERE ARE 49 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

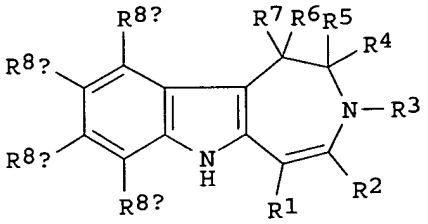
L3 ANSWER 12 OF 35 CAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 13 Mar 2005
ACCESSION NUMBER: 2005:220132 CAPLUS
DOCUMENT NUMBER: 142:298092
TITLE: Preparation of azepino[4,5-b]indole derivatives as modulators of nuclear receptors
INVENTOR(S): Busch, Brett; Flatt, Brenton T.; Gu, Xiao-Hui; Martin, Richard; Mohan, Raju; Wang, Tie-Lin; Wu, Jason H.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 106 pp., Cont.-in-part of U.S. Ser. No. 447,302.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2005054634	A1	20050310	US 2003-895431	20031202
US 2004023947	A1	20040205	US 2003-447302	20030527
WO 2005056554	A2	20050623	WO 2004-US40352	20041201
WO 2005056554	A3	20050818		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:	US 2002-383574P	P	20020524
	US 2003-447302	A2	20030527
	US 2003-895431	A	20031202

OTHER SOURCE(S): MARPAT 142:298092
GI



I

AB The title compds. (I) [R1 = -C(J)OR14, -C(J)SR14, (un)substituted -C(J)NH2; J = O, S, (un)substituted NH; R2 = H, halo, (un)substituted alkyl; R3 = -C(O)R9; R4, R5, R6 and R7 are together selected from (a), (b), etc. below: (a) R4, R5 = H or halo and R6, R7 = halo, each (un)substituted alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, aryl, aralkyl, heteroaryl, or heteroaralkyl, etc.; or R6 and R7, together with the carbon atom to which they are attached, form each (un)substituted cycloalkyl, heterocyclyl, cycloalkenyl, alkylidene, cycloalkylidene, heterocyclylidene, aralkylidene or substituted heteroaralkylidene; (b) R4, R5 = halo, each (un)substituted alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, aryl, heteroaryl, or heteroaralkyl, etc.; or R4 and R5, together with the carbon atom to which they are attached, form (un)substituted cycloalkyl, heterocyclyl, cycloalkenyl, alkylidene, cycloalkylidene, heterocyclylidene, aralkylidene or heteroaralkylidene, and R6, R7 = H or halo; R8a, R8b, R8c, R8d = H, halo, pseudohalo, cyano, azido, amidino, guanidino, each (un)substituted alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, aryl, aralkyl, heteroaryl, or heteroaralkyl, etc.; R14 = each (un)substituted alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, etc.] are prepared These compds. modulate nuclear receptors, in particular farnesoid X receptor and are agonists, partial agonists, inverse agonists, partial antagonists, or antagonists of farnesoid X receptor. They are useful for the treatment, prevention, or amelioration of one or more symptoms of disease or disorder directly or indirectly related to the activity of the above receptors, including hyperlipidemia, hypercholesterolemia, hypertriglyceridemia, dyslipidemia, lipodystrophy, atherosclerosis, atherosclerotic disease, atherosclerotic disease events, atherosclerotic cardiovascular disease, Syndrome X, diabetes mellitus, type II diabetes, insulin insensitivity, hyperglycemia, cholestasis and **obesity.** Thus, to a solution of Et 1,2,3,6-tetrahydroazepino[4,5-b]indole-5-carboxylate (52 mg, 0.2 mmol) in CH2Cl2 was added 4-fluorobenzoyl chloride (36 μL, 0.2 mmol) and TEA (56 μL, 0.4 mmol) and the mixture was shaken overnight at 20°, treated with Trisamine resin (50 mg), and shaken for 2 h at 20°. The resin was removed by filtration through a Florisil cartridge. Evaporation of solvent gave a crude product, which was purified by trituration with methanol to give Et 3-(4-fluorobenzoyl)-1,2,3,6-tetrahydroazepino[4,5-b]indole-5-carboxylate. Et 3-(3,4-difluorobenzoyl)-1-methyl-1,2,3,6-tetrahydroazepino[4,5-b]indole-5-carboxylate was administered daily by oral gage for 7 days to young adult male mice. Plasma total cholesterol and triglyceride levels were significantly lowered.

IT **151126-32-8**, Pramlintide
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(coadministration; preparation of azepino[4,5-b]indole derivs. as modulators of nuclear receptors, in particular farnesoid X receptor)

L3 ANSWER 13 OF 35 CAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 11 Mar 2005
ACCESSION NUMBER: 2005:216700 CAPLUS
DOCUMENT NUMBER: 142:274080
TITLE: Methods for treating or ameliorating ghrelin-associated diseases and disorders
INVENTOR(S): Baron, Alain; Young, Andrew A.; Gedulin, Bronislava
PATENT ASSIGNEE(S): Amylin Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 44 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005021026	A2	20050310	WO 2004-US28283	20040830
WO 2005021026	A3	20050414		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:			
	US 2003-498898P	P	20030829
	US 2004-554528P	P	20040318

AB Methods for modulating the effective levels of ghrelin are disclosed. These methods include the use of amylin, amylin agonists and amylin antagonists to regulate the effective levels of ghrelin. Methods for the prevention, treatment, or amelioration of ghrelin-associated diseases or disorders utilizing the methods for modulating ghrelin are also disclosed.

IT **151126-32-8**, Pramlintide
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods for treating or ameliorating ghrelin-associated diseases and disorders)

L3 ANSWER 14 OF 35 CAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 01 Dec 2004
ACCESSION NUMBER: 2004:1027457 CAPLUS
DOCUMENT NUMBER: 142:367965
TITLE: Amylin replacement with pramlintide as an adjunct to insulin therapy improves long-term glycemic and weight control in type 1 diabetes mellitus: a 1-year, randomized controlled trial

AUTHOR(S): Ratner, R. E.; Dickey, R.; Fineman, M.; Maggs, D. G.; Shen, L.; Strobel, S. A.; Weyer, C.; Kolterman, O. G.
CORPORATE SOURCE: Medstar Clinical Research, Washington, DC, USA
SOURCE: Diabetic Medicine (2004), 21(11), 1204-1212
CODEN: DIMEEV; ISSN: 0742-3071
PUBLISHER: Blackwell Publishing Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The autoimmune-mediated destruction of pancreatic β-cells in Type 1 diabetes mellitus renders patients deficient in two glucoregulatory peptide hormones, insulin and amylin. With insulin replacement alone, most patients do not achieve glycemic goals. We aimed to determine the long-term efficacy and safety of adjunctive therapy with pramlintide, a synthetic human amylin analog, in patients with Type 1 diabetes. In a double-blind, placebo-controlled, parallel-group, multicenter study, 651 patients with Type 1 diabetes (age 41 ± 13 years, HbA1c 8.9 ± 1.0%, mean ± SD) were randomized to mealtime injections of placebo or varying doses of pramlintide, in addition to their insulin therapy, for 52 wk. Addition of pramlintide [60 μg three times daily (TID) or four times daily (QID)] to insulin led to significant redns. in HbA1c from baseline to Week 52 of 0.29% ($P < 0.011$) and 0.34% ($P < 0.001$), resp., compared with a 0.04% reduction in placebo group. Three times the proportion of pramlintide- than placebo-treated patients achieved an HbA1c of < 7%. The greater reduction in HbA1c with pramlintide was achieved without an increase in concomitant insulin use and was accompanied by a significant **reduction** in **body weight** from baseline to Week 52 of 0.4 kg in the 60 μg TID ($P < 0.027$) or QID ($P < 0.040$) pramlintide treatment groups, compared with a 0.8-kg **gain** in body **weight** in the placebo group. The most common adverse event in pramlintide-treated patients was transient, mild-to-moderate nausea. These results show that mealtime amylin replacement with pramlintide, as an adjunct to insulin therapy, improves long-term glycemic and weight control in patients with Type 1 diabetes.

IT **151126-32-8**, Pramlintide
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(amylin replacement with pramlintide as adjunct to insulin therapy in type 1 diabetes mellitus)

REFERENCE COUNT: 34 THERE ARE 34 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 15 OF 35 CAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 08 Oct 2004
ACCESSION NUMBER: 2004:822389 CAPLUS
DOCUMENT NUMBER: 142:107473
TITLE: Insulin therapy in type 2 diabetes
AUTHOR(S): Davis, Trent; Edelam, Steven V.
CORPORATE SOURCE: Section of Diabetes/Metabolism, Veterans Affairs San Diego HealthCare System, San Diego, CA, 92161, USA
SOURCE: Medical Clinics of North America (2004), 88(4), 865-895
CODEN: MCNAA9; ISSN: 0025-7125
PUBLISHER: Elsevier Inc.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. Type 2 diabetes is a common disorder often accompanied by

numerous metabolic abnormalities leading to elevated rates of cardiovascular morbidity and mortality. Improved glycemia will delay or prevent the development of microvascular disease and reduce many or all of the acute and subacute complications that worsen the quality of daily life. Exogenous insulin is usually the last line of treatment used to normalize glycosylated Hb in patients with type 2 diabetes who have failed other therapeutic modalities. In selected patients, combination therapy with insulin and oral antidiabetic medications can be an effective method for normalizing glycemia without the need for rigorous insulin regimens. Bedtime intermediate- and long acting-insulin are administered and progressively increased until the fasting blood glucose concentration is normalized. Addnl. benefits of combination therapy include ease of administration, excellent patient compliance and safety, and lower exogenous insulin requirements with less peripheral hyperinsulinemia and **weight gain.** If combination therapy is not successful, a split-mixed regimen of an intermediate- and a fast-acting insulin equally divided between the pre-breakfast and pre-dinner periodos can be effective especially in **obese** patients. For patients who do not achieve glucose control on combination or split-mixed regimens, an intensive basal bolus multiple-injection regimen is indicated. Continuous s.c. insulin infusion pumps can be particularly useful in treating patients with type 2 diabetes mellitus who do not respond satisfactorily to more conventional treatment strategies. The use of fast-acting insulin analogs should be used in the majority of insulin-requiring diabetics because of its more physiol. pharmacokinesis. Inhaled insulin and the amylin analog pramlintide also hold promise to intensively control glycemia in patients with insulin-requiring type 2 diabetes. The glycemic objectives for patients with type 2 diabetes should be similar to those for patients with type 1 diabetes, namely, to normalize glycemia and glycosylated Hb without causing undue **weight gain** or hypoglycemia or adversely affecting the quality of daily life. This is best achieved in a multidisciplinary setting using complementary therapeutic modalities that include a combination of diet, exercise, and pharmacol. therapy. Emphasis should be placed on diet and exercise initially, and throughout the course of management as well, since even modest success with these therapies will enhance the glycemic response to both oral antidiabetic agents and insulin.

IT **151126-32-8**, Pramlintide
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(insulin therapy in type 2 diabetes)

REFERENCE COUNT: 80 THERE ARE 80 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 16 OF 35 CAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 24 May 2004
ACCESSION NUMBER: 2004:418027 CAPLUS
DOCUMENT NUMBER: 141:64911
TITLE: Effect of pramlintide on weight in overweight and **obese** insulin-treated type 2 diabetes patients
AUTHOR(S): Hollander, Priscilla; Maggs, David G.; Ruggles, James A.; Fineman, Mark; Shen, Larry; Kolterman, Orville G.; Weyer, Christian
CORPORATE SOURCE: Baylor College of Medicine, Dallas, TX, USA
SOURCE: Obesity Research (2004), 12(4), 661-668
CODEN: OBREFR; ISSN: 1071-7323

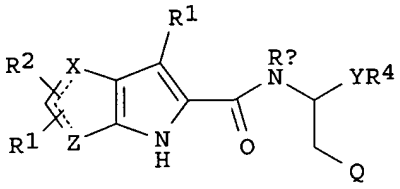
PUBLISHER: North American Association for the Study of Obesity
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Objective: Several randomized, placebo-controlled, double-blind trials in insulin-treated patients with type 2 diabetes have shown that adjunctive therapy with pramlintide reduces HbA1c with concomitant weight loss. This anal. further characterizes the weight-lowering effect of pramlintide in this patient population. Research Methods and Procedures: This pooled post hoc anal. of two long-term trials included all patients who were overweight/**obese** at baseline (BMI > 25 kg/m2), and who were treated with either 120 μg pramlintide BID (n = 254; HbA1c 9.2%; weight, 96.1 kg) or placebo (n = 244; HbA1c 9.4%; weight, 95.0 kg). Statistical endpoints included changes from baseline to week 26 in HbA1c, body weight, and insulin use. Results: Pramlintide treatment resulted in significant redns. from baseline to week 26, compared with placebo, in HbA1c and body weight (both, $p < 0.0001$), for placebo-corrected redns. of -0.41% and -1.8 kg, resp. Approx. three times the number of patients using pramlintide experienced a ≥5% **reduction** of **body wt** . than with placebo (9% vs. 3%, $p = 0.0005$). Patients using pramlintide also experienced a proportionate decrease in total daily insulin use ($r = 0.39$, $p < 0.0001$). The greatest placebo-corrected redns. in weight at week 26 were observed in pramlintide-treated patients with a BMI >40 kg/m2 and in those concomitantly treated with metformin (both, $p < 0.001$), for placebo-corrected redns. of -3.2 kg and -2.5 kg, resp. Discussion: These findings support further evaluation of the weight-lowering potential of pramlintide in **obese** patients with type 2 diabetes.
IT **151126-32-8**, Pramlintide
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pramlintide effect on weight in overweight and **obese** insulin-treated type 2 diabetes patients)
REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 17 OF 35 CAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 26 Feb 2004
ACCESSION NUMBER: 2004:157498 CAPLUS
DOCUMENT NUMBER: 140:199313
TITLE: Preparation of fused pyrrolylcarboxamides as glycogen phosphorylase inhibitors
INVENTOR(S): Daisy, Joe
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: Eur. Pat. Appl., 71 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1391460	A1	20040225	EP 2003-20676	20000918
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY				
EP 1088824	A2	20010404	EP 2000-308131	20000918
EP 1088824	A3	20010627		

EP 1088824	B1	20040107			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO					
US 2002183369	A1	20021205	US 2002-117370		20020405
US 6576653	B2	20030610			
US 2003195361	A1	20031016	US 2003-367002		20030214
US 6828343	B2	20041207			
PRIORITY APPLN. INFO.:			US 1999-157148P	P	19990930
			EP 2000-308131	A3	20000918
			US 2000-670759	A3	20000927
			US 2002-117370	A3	20020405

OTHER SOURCE(S): MARPAT 140:199313
GI



I

AB Title compds. [I; Q = substituted aryl, heteroaryl; Z, X = C, CH, CH2, N, O, S; X1 = NRa, CH2, O , S; dotted lines = bond, null; both dotted lines are not simultaneously bonds; R1 = H, halo, alkoxy, alkylthio, alkyl, CF3, NH2, alkylamino, dialkylamino, NO2, CN, CO2H, carboxyalkyl, alkenyl, alkynyl; Ra, Rb = H, alkyl; Y = CH(OH), null; R2R3 = atoms to form a 5-6 membered ring containing 0-3 heteroatoms and 0-2 double bonds; R4 = COA; A = NRdRd, NRaCH2CH2ORa, N-heterocyclyl; Rd = H, alkyl, alkoxy, aryl, (substituted) aryl, heteroaryl; Rc = H, CO2Ra, ORa, SRa, NRaRa; n = 1-3], were prepared for treatment of diabetes, insulin resistance, diabetic neuropathy, diabetic nephropathy, diabetic retinopathy, cataracts, hyperglycemia, hypercholesterolemia, hypertension, hyperinsulinemia, hyperlipidemia, atherosclerosis, or tissue ischemia (no data). Thus, 6H-thieno[2,3-b]pyrrole-5-carboxylic acid and (3S)-amino-1-((3R,4S)-dihydroxypyrrolidin-1-yl)-(2R)-hydroxy-4-phenylbutan-1-one were coupled using 4-(dimethylamino)pyridine, 1-hydroxybenzotriazole hydrate and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride in CH2Cl2/DMF to give 6H-thieno[2,3-b]pyrrole-5-carboxylic acid [(1S)-benzyl-3-((3R,4S)-dihydroxypyrrolidin-1-yl)-(2R)-hydroxy-3-oxopropyl]amide.

IT **187887-46-3**, Symlin
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(coadministration; preparation of fused pyrrolylcarboxamides as glycogen phosphorylase inhibitors)

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 18 OF 35 CAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 05 Jan 2004
ACCESSION NUMBER: 2004:5054 CAPLUS

DOCUMENT NUMBER: 140:53765
TITLE: Addition of pramlintide to insulin therapy lowers HbA1c in conjunction with weight loss in patients with type 2 diabetes approaching glycaemic targets
AUTHOR(S): Hollander, P.; Ratner, R.; Fineman, M.; Strobel, S.; Shen, L.; Maggs, D.; Kolterman, O.; Weyer, C.
CORPORATE SOURCE: Baylor University Medical Center, Dallas, TX, USA
SOURCE: Diabetes, Obesity and Metabolism (2003), 5(6), 408-414
CODEN: DOMEF6; ISSN: 1462-8902
PUBLISHER: Blackwell Publishing Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Aim: Two long-term, randomized, double-blind, placebo-controlled clin. trials in insulin-using patients with type 2 diabetes, spanning a wide range of baseline glycemic control, have shown that the addition of pramlintide, an analog of the β-cell hormone amylin, to pre-existing insulin regimens results in redns. in HbA1c that are accompanied by weight loss. Methods: To assess whether this profile of pramlintide is observed in patients approaching, but not yet reaching, glycemic targets, we conducted a pooled post hoc anal. of the two trials, including all patients with an entry HbA1c between 7.0 and 8.5%. Within this subset of patients, 80 were treated with placebo + insulin [baseline HbA1c 8.0±0.3%, weight 87.3±19.3 kg (mean ± s.d.)] and 86 with pramlintide (120 μg bid) + insulin [HbA1c 8.0±0.4%, weight 92.5±20.4 kg (mean ± s.d.)]. Endpoints included changes from baseline to Week 26 in HbA1c, body weight, and the event rate of severe hypoglycemia. Results: Adjunctive therapy with pramlintide resulted in significant redns. in both HbA1c and body weight from baseline to week 26 (-0.43% and -2.0 kg differences from placebo, resp., both $p < 0.001$). These changes were achieved without a concomitant increase in the overall rate of severe hypoglycemic events (0.13 pramlintide vs. 0.19 placebo, events/patient year of exposure). Conclusions: The data from this post hoc anal. indicate that the addition of pramlintide to insulin therapy may help patients with type 2 diabetes who are approaching, but not yet reaching, glycemic targets to achieve further redns. in HbA1c without concomitant **weight gain** and increased risk of severe hypoglycemia.

IT **151126-32-8**, Pramlintide
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(addition of pramlintide to insulin therapy lowers HbA1c in conjunction with weight loss in patients with type 2 diabetes approaching glycemic targets)

REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

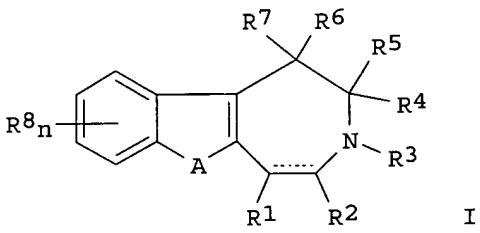
L3 ANSWER 19 OF 35 CAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 07 Dec 2003
ACCESSION NUMBER: 2003:951028 CAPLUS
DOCUMENT NUMBER: 140:16715
TITLE: Preparation of azepinoindole and pyridoindole derivatives as modulators of farnesoid X and/or orphan nuclear receptors
INVENTOR(S): Martin, Richard; Wang, Tie-Lin; Flatt, Brenton Todd; Gu, Xiao-Hui; Griffith, Ronald
PATENT ASSIGNEE(S): X-Ceptor Therapeutics, Inc., USA
SOURCE: PCT Int. Appl., 268 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003099821	A1	20031204	WO 2003-US16767	20030527
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2485909	AA	20031204	CA 2003-2485909	20030527
AU 2003243328	A1	20031212	AU 2003-243328	20030527
EP 1532153	A1	20050525	EP 2003-755523	20030527
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
JP 2005531585	T2	20051020	JP 2004-507478	20030527

PRIORITY APPLN. INFO.: US 2002-383574P P 20020524
WO 2003-US16767 W 20030527

OTHER SOURCE(S): MARPAT 140:16715
GI



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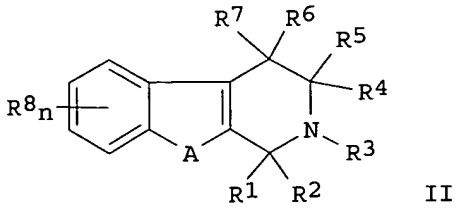


II

AB The present invention is directed to azepinoindole and pyridoindole derivs. (shown as I and II; variables defined below; e.g. Et 1,2,3,6-tetrahydroazepino[4,5-b]indole-5-carboxylate). These compds. were used in pharmaceutical compns. and methods for modulating the activity of farnesoid X receptor and/or orphan nuclear receptors. A farnesoid X receptor/ECREx7 co-transfection assay and a TR-FRET assay

were used to establish the EC50/IC50 values for potency and percent activity or inhibition for efficacy; efficacy defines the activity of a compound relative to a high control (chenodeoxycholic acid, CDCA) or a low control (DMSO/vehicle). Most of the compds. disclosed and tested exhibited activity in at least one of the assays (EC50 or IC50 <10 μM); most showed activity at <1 μM, e.g. Pr 3-(4-fluorobenzoyl)-2-methyl-1,2,3,6-tetrahydroazepino[4,5-b]indole-5-carboxylate exhibited agonist activity <1 μM EC50 and >100 % efficacy and 8-(3-cyclopropyl-1-methylureido)-3-(4-fluorobenzoyl)-1,1-dimethyl-1,2,3,6-tetrahydroazepino[4,5-b]indole-5-carboxylic acid Et ester exhibited antagonist activity with IC50 <100 nM and 100 % inhibition. Although the methods of preparation are not claimed, 74 example prepns. of I and II and characterization data for many more I and II are included. For I and II: n = 0-4; A is -N(R9)-, -O- or -S(O)t- (t = 0-2); R1 and R2 = H, alkyl, alkenyl, alkynyl, aryl, heteroaryl, cycloalkyl, heterocyclyl, aralkyl, heteroaralkyl, -OR14, -SR14, -N(R15)R16, -N(R15)S(O)2R43; -N(R17)N(R15)R16, -N(R17)N(R15)S(O)2R43, -C(O)R18, -C(O)OR14, -C(S)OR14, -C(O)SR14, -C(O)N(R15)R16, -C(O)N(R15)S(O)2R43, -C(O)N(R15)N:R16 and -C(O)N(R17)N(R15)R16; or -C(O)N(R17)N(R15)S(O)2R43; or R1 and R2, together with the atom to which they are attached, form a cycloalkyl, heterocyclyl, aryl, or heteroaryl ring. R3 is H, alkyl, alkenyl, alkynyl, cycloalkyl, aryl, aralkyl, heteroaryl, heterocyclyl, heteroaralkyl, -C(O)R10, -C(O)OR10, -S(O)2R10, -C(O)N(R11)R12, -C(O)N(R11)S(O)2R43, -C(O)N(R13)N(R11)R12, -C(O)N(R13)N(R11)S(O)2R43, -N(R13)C(O)R10, -N(R13)C(O)N(R11)R12, -N(R13)C(O)N(R11)S(O)2R43, -N(R10)C(O)N(R13)N(R11)R12, -N(R10)C(O)N(R13)N(R11)S(O)2R43, -N(R13)C(O)OR10, -P(O)OR10, or -P(O)(OR19)OR12. R4, R5, R6 and R7 = H, alkyl, alkenyl, alkynyl, aryl, heteroaryl, cycloalkyl, heterocyclyl, aralkyl, heteroaralkyl, -OR14, -SR14, -S(O)2R14, -N(R15)R16, -N(R15)S(O)2R43, -C(O)R18, -C(O)OR20, -C(O)N(R21)R22, -C(O)N(R21)S(O)2R43; -C(O)N(R42)N(R21)R22; or -C(O)N(R42)N(R21)S(O)2R43; or R4 and R5, or R4 and R6, or R4 and R7, or R5 and R6, or R5 and R7, or R6 and R7, together with the C atom to which they are attached, form a cycloalkyl, heterocyclyl, or cycloalkenyl ring, or together form a double bond and the others of R4, R5, R6 and R7 are as described above; or R6 and R7 together form an oxo, thioxo, imine, oxime or a hydrazone, or R6 and R7, together with the C atom to which they are attached, form an exocyclic double bond, and R4 and R5 are as described above. R8 = alkyl, alkenyl, alkynyl, aryl, heteroaryl, cycloalkyl, heterocyclyl, halo, pseudohalo, cyano, nitro, -C(O)OR23, -C(O)N(R24)R25, -C(O)N(R24)S(O)2R43, -C(O)R26, -OR27, -SR27, -C(S)OR23, -C(O)SR23, -N(R28)R29, and -N(R28)S(O)2R43, or two adjacent R8 groups, together with the carbons to which they are attached, form an aryl, cycloalkyl, heterocyclyl or heteroaryl; addnl. details including provisos are given in the claims.

IT **151126-32-8**, Pramlintide
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(codrug; preparation of azepinoindole and pyridoindole derivs. as modulators of farnesoid X and/or orphan nuclear receptors)

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 20 OF 35 CAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 03 Dec 2003
ACCESSION NUMBER: 2003:940514 CAPLUS
DOCUMENT NUMBER: 140:229044
TITLE: Effect of pramlintide on A1C and body weight in insulin-treated African Americans and Hispanics with type 2 diabetes: a pooled post hoc analysis

AUTHOR(S): Maggs, D.; Shen, L.; Strobel, S.; Brown, D.; Kolterman, O.; Weyer, C.
CORPORATE SOURCE: Amylin Pharmaceuticals, Inc., San Diego, CA, 92121, USA
SOURCE: Metabolism, Clinical and Experimental (2003), 52(12), 1638-1642
CODEN: METAAJ; ISSN: 0026-0495
PUBLISHER: W. B. Saunders Co.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB An unresolved problem in the management of type 2 diabetes is that improvement of glycemic control with insulin, insulin secretagogues, and insulin sensitizers is often accompanied by undesired **wt . gain.** This problem is of particular concern in ethnic groups with a high propensity for diabetes and **obesity**, such as African Americans and Hispanics. Two 1-yr, randomized, double-blind, placebo-controlled clin. trials in insulin-treated patients with type 2 diabetes have shown that adjunctive therapy with pramlintide, an analog of the human β-cell hormone amylin, reduces A1C with concomitant weight loss, rather than **weight gain.** To assess the effect of pramlintide in various ethnic groups with type 2 diabetes using insulin, we conducted a pooled post hoc anal. of the 2 trials, which included all Caucasian (n = 315), African American (n = 47), and Hispanic (n = 48) patients (age 57 yr, A1C 9.1%, body mass index [BMI] 33 kg/m2, mean values) who completed 52 wk of treatment with either pramlintide (120 μg twice daily or 150 μg 3 times a day) or placebo. Primary endpoints included changes from baseline to week 52 in A1C and body weight Collectively, pramlintide-treated patients achieved significant redns. from baseline in both A1C and body weight (placebo-corrected treatment effects at week 52: -0.5% and -2.6 kg, resp., both P <.0001). The simultaneous **reduction** in A1C and **body weight** at week 52 was evident across all 3 ethnic groups and appeared to be most pronounced in African Americans (-0.7%, -4.1 kg), followed by Caucasians (-0.5%, -2.4 kg) and Hispanics (-0.3%, -2.3 kg). The glycemic improvement with pramlintide was not associated with an increased incidence of hypoglycemia over the entire study period (43% pramlintide v 40% placebo). Nausea, the most common adverse event associated with pramlintide treatment, was mostly mild and confined to the first 4 wk of therapy (25% pramlintide v 16% placebo) with comparable patterns in the 3 ethnic groups. Thus, pending further experience, the combined improvement in glycemic and weight control with pramlintide treatment appears to be generalizable to a broad population of mixed ethnicity.
IT **151126-32-8**, Pramlintide
RL: ADV (Adverse effect, including toxicity); DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effect of pramlintide on A1C and body weight in insulin-treated African Americans and Hispanics with type 2 diabetes)
REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 21 OF 35 CAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 11 Jul 2003
ACCESSION NUMBER: 2003:532326 CAPLUS
DOCUMENT NUMBER: 139:63796
TITLE: Use of amylin agonists to modulate triglycerides
INVENTOR(S): Kolterman, Orville G.; Weyer, Christian; Maggs, David G.; Fineman, Mark

PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 12 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003130177	A1	20030710	US 2003-337979	20030108
CA 2475173	AA	20030717	CA 2003-2475173	20030108
WO 2003057244	A2	20030717	WO 2003-US369	20030108
WO 2003057244	A3	20031218		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2003235742	A1	20030724	AU 2003-235742	20030108
EP 1474164	A2	20041110	EP 2003-729360	20030108
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				

PRIORITY APPLN. INFO.: US 2002-347128P P 20020108
WO 2003-US369 W 20030108

AB Methods of improving lipid profile, including methods for lowering fasting triglyceride levels and post-prandial triglyceride excursions are disclosed comprising administering an effective amount of an amylin or amylin agonist.

IT **151126-32-8**, Pramlintide
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of amylin agonists to improve lipid profiles)

L3 ANSWER 22 OF 35 CAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 18 Apr 2003
ACCESSION NUMBER: 2003:300597 CAPLUS
DOCUMENT NUMBER: 138:314591
TITLE: Methods for affecting various diseases utilizing LXR compounds
INVENTOR(S): Schulman, Ira G.; Bischoff, Eric D.; Tangirala, Rajendra K.
PATENT ASSIGNEE(S): CA13821314591D, USA
SOURCE: U.S. Pat. Appl. Publ., 33 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

US 2003073614	A1	20030417	US 2001-982544	20011017
US 6924311	B2	20050802		
US 2005267013	A1	20051201	US 2005-159653	20050623
PRIORITY APPLN. INFO.:			US 2001-982544	A1 20011017

AB The invention relates to methods for elevating high d. lipoprotein (HDL) plasma levels, decreasing the absorption of dietary cholesterol in the intestine, decreasing the plasma level of low d. lipoprotein (LDL), and increasing the conversion of cholesterol to bile acids, utilizing LXRβ selective agonists, usually without elevating the plasma levels of triglycerides. Also provided are methods of using such agonists to treat metabolic diseases alone or in combination with other active agents. Also provided are methods for decreasing hyperglycemia and insulin resistance methods for treating type II diabetes, and methods for treating type II diabetes and reducing the cardiovascular complications of type II diabetes, utilizing an LXR agonist. Further provided are methods for treating **obesity** and methods for treating the complications of **obesity** including type II diabetes, cardiovascular disease, hyperlipidemia, and hypertension, administering an LXRα-selective antagonist.

IT **151126-32-8**, Pramlintide
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treatment of various diseases utilizing LXR compds.)

REFERENCE COUNT: 65 THERE ARE 65 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 23 OF 35 CAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 19 Feb 2003
ACCESSION NUMBER: 2003:123910 CAPLUS
DOCUMENT NUMBER: 138:231209
TITLE: Weight effect of current and experimental drugs for diabetes mellitus: From promotion to alleviation of **obesity**
AUTHOR(S): Purnell, Jonathan Q.; Weyer, Christian
CORPORATE SOURCE: Division of Endocrinology, Diabetes, and Clinical Nutrition, Oregon Health and Science University, Portland, OR, USA
SOURCE: Treatments in Endocrinology (2003), 2(1), 33-47
CODEN: TERNAN; ISSN: 1175-6349
PUBLISHER: Adis International Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. Two landmark intervention studies, the Diabetes Control and Complications Trial (DCCT) in patients with type 1 diabetes mellitus and the United Kingdom Prospective Diabetes Study (UKPDS) in patients with type 2 diabetes mellitus, have unequivocally demonstrated that intensive diabetes therapy reduces the risk of long-term diabetic complications. As a result, the commonly accepted treatment goal for most patients with diabetes is the achievement and maintenance of glycemic control that is as close to the normal range as safely possible. Important adverse effects of intensive diabetes therapy, particularly when the treatment includes insulin or several of the oral antihyperglycemic agents, are an increased risk of hypoglycemia and undesired **weight gain.** Improvement of glycemic control with insulin, insulin secretagogues (sulfonylureas, meglitinides), and insulin sensitizers (thiazolidinediones) is often accompanied by **weight gain.** The etiol. of this **weight gain** is likely multifaceted, including a reduction

of glucosuria, increased caloric intake to prevent hypoglycemia, and anabolic effects on adipose tissue. Biguanides and α-glucosidase inhibitors have a neutral or even pos. effect (decrease) on weight, which may partly be attributable to their non-insulinotropic mechanism of action, a modest effect on satiety, and to their gastrointestinal adverse effect profile. Several antihyperglycemic agents that are currently in clin. development may improve glycemic control in conjunction with weight reduction These include an analog of the pancreatic β-cell hormone amylin (pramlintide), as well as glucagon-like peptide-1 (GLP-1) and exendin, and their analogs. Pharmacol. agents with antihyperglycemic and pos. weight effects have the potential to become important addns. to our therapeutic armamentarium, in that they may help to achieve glycemic targets while addressing the long-standing clin. problem of **wt . gain** as an adverse effect of intensive diabetes therapy.

IT **151126-32-8**, Pramlintide
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antihyperglycemic drugs-related **wt gain** in patients with diabetes mellitus)

REFERENCE COUNT: 166 THERE ARE 166 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 24 OF 35 CAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 10 Sep 2002
ACCESSION NUMBER: 2002:680698 CAPLUS
DOCUMENT NUMBER: 137:211050
TITLE: Pramlintide: an agent for glycemic control plus weight control?
AUTHOR(S): Riddle, Matthew C.
CORPORATE SOURCE: Department of Medicine, Division of Endocrinology, Diabetes, & Clinical Nutrition, Oregon Health & Science University, Portland, OR, USA
SOURCE: Diabetes Technology & Therapeutics (2002), 4(1), 63-65
CODEN: DTTHFH; ISSN: 1520-9156
PUBLISHER: Mary Ann Liebert, Inc.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. Pramlintide, an amylin analog, improves glycemic control and results in weight loss in insulin requiring type 2 diabetics. This review includes details of a previous clin. trial by Ratner along with discussion of the outcome and limitations of this study. The arrival of pramlintide may herald the development of more therapeutic analogs from dozens of peptides produced by neuroendocrine cells of the gastrointestinal tract as well as the central nervous system.

IT **151126-32-8**, Pramlintide
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pramlintide for glycemic control plus weight control)

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 25 OF 35 CAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 10 Sep 2002
ACCESSION NUMBER: 2002:680696 CAPLUS
DOCUMENT NUMBER: 137:211181
TITLE: Adjunctive therapy with the amylin analogue

pramlintide leads to a combined improvement in glycemic and weight control in insulin-treated subjects with type 2 diabetes

AUTHOR(S): Ratner, Robert E.; Want, Laura L.; Fineman, Mark S.; Velte, Maggie J.; Ruggles, James A.; Gottlieb, Alan; Weyer, Christian; Kolterman, Orville G.

CORPORATE SOURCE: Medstar Research Institute, Washington, DC, USA

SOURCE: Diabetes Technology & Therapeutics (2002), 4(1), 51-61
CODEN: DTTHFH; ISSN: 1520-9156

PUBLISHER: Mary Ann Liebert, Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The objective of this study was to assess the effect of mealtime amylin replacement with pramlintide on long-term glycemic and weight control in subjects with type 2 diabetes. This 52-wk, randomized, placebo-controlled, multicenter, double-blind, dose-ranging study in 538 insulin-treated subjects with type 2 diabetes compared the efficacy and safety of 30-, 75-, or 150-μg doses of pramlintide, a synthetic analog of the β-cell hormone amylin, to placebo when injected s.c. three times daily (TID) with major meals. Pramlintide therapy led to a mean reduction in HbA1c of 0.9% and 1.0% from baseline to week 13 in the 75- and 150-μg dose groups, which was significant compared to placebo ($p = 0.0004$ and $p = 0.0002$, resp.). In the 150-μg dose group, there was a mean reduction in HbA1c of 0.6% from baseline to week 52 ($p = 0.0068$ compared to placebo). The greater reduction in HbA1c with pramlintide was achieved without increases in insulin use or severe hypoglycemia, and was accompanied by a significant ($p < 0.05$) **reduction** in **body weight** in all dose groups compared to placebo. Three times the proportion of subjects in the 150-μg pramlintide group compared to the placebo group achieved a concomitant reduction in both HbA1c and body weight from baseline to week 52 (48% vs. 16%). The most common adverse event reported with pramlintide treatment was nausea, which was mild to moderate and dissipated early in treatment. The results from this study support the safety and efficacy of pramlintide administered three times a day with major meals, in conjunction with insulin therapy, for improving long-term glycemic and weight control in subjects with type 2 diabetes.

IT **151126-32-8**, Pramlintide
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(adjunctive therapy with amylin analog pramlintide leads to a combined improvement in glycemic and weight control in insulin-treated subjects with type 2 diabetes)

REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 26 OF 35 CAPLUS COPYRIGHT 2006 ACS on STN

ED Entered STN: 20 Aug 2002

ACCESSION NUMBER: 2002:625547 CAPLUS

DOCUMENT NUMBER: 137:179976

TITLE: Unresolved challenges with insulin therapy in type 1 and type 2 diabetes: potential benefit of replacing amylin, a second β-cell hormone

AUTHOR(S): Edelman, S. V.; Weyer, C.

CORPORATE SOURCE: Veteran's Affairs Health Care Systems, University of California, San Diego, CA, USA

SOURCE: Diabetes Technology & Therapeutics (2002), 4(2),

175-189
CODEN: DTTHFH; ISSN: 1520-9156
PUBLISHER: Mary Ann Liebert, Inc.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. Current insulin therapy still fails to safely restore near-normoglycemia in the majority of patients. Among the barriers to achieving tight long-term glycemic control with insulin in both type 1 and type 2 diabetes are an increased risk of hypoglycemia, undesired **weight gain**, and a failure to normalize postprandial hyperglycemia and excessive unpredictable diurnal glucose fluctuations. Amylin is a second β-cell hormone that is cosecreted with insulin in response to meals, and is deficient in patients with type 1 and insulin-requiring type 2 diabetes. Preclin. studies indicate that amylin acts as a neuroendocrine hormone that complements the effects of insulin in postprandial glucose regulation by suppressing postprandial glucagon secretion and slowing the rate of nutrient delivery from the stomach to the small intestine. Human amylin is not optimal for replacement therapy because of its propensity to aggregate; thus, pramlintide, a soluble, nonaggregating synthetic peptide analog of human amylin, was developed that has potency at least equal to that of human amylin. In clin. studies, s.c. injections of pramlintide prior to meals, in addition to insulin therapy, significantly reduced postprandial glucose excursions and lowered HbA1c levels in patients with type 1 and type 2 diabetes. The improvement in long-term glycemic control was associated with a significant **reduction** in **body weight** and occurred without increases in total daily insulin use or in overall severe hypoglycemia event rates. Because of this unique spectrum of clin. effects, amylin replacement with pramlintide as an adjunctive therapy to insulin is a promising approach that may fulfill some of the unmet clin. needs of insulin-using patients with type 1 and type 2 diabetes.

IT **151126-32-8**, Pramlintide
RL: ADV (Adverse effect, including toxicity); DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(insulin therapy in type 1 and type 2 diabetes mellitus patients: potential benefit of replacing amylin, a second β-cell hormone)

REFERENCE COUNT: 98 THERE ARE 98 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 27 OF 35 CAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 01 May 2002
ACCESSION NUMBER: 2002:322586 CAPLUS
DOCUMENT NUMBER: 137:242215
TITLE: Novel peptides under development for the treatment of type 1 and type 2 diabetes mellitus
AUTHOR(S): Baron, Alain D.; Kim, Dennis; Weyer, Christian
CORPORATE SOURCE: Amylin Pharmaceuticals, Inc., San Diego, CA, 92121, USA
SOURCE: Current Drug Targets: Immune, Endocrine and Metabolic Disorders (2002), 2(1), 63-82
CODEN: CDTIBT; ISSN: 1568-0088
PUBLISHER: Bentham Science Publishers Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. Recent availability of expanded treatment options for both

type 1 and type 2 diabetes has not translated into easier and significantly better glycemic and metabolic management. Patients with type 1 diabetes continue to experience increased risk of hypoglycemic episodes and progressive **weight gain** resulting from intensive insulin treatment, despite the recent availability of a variety of insulin analog. Given the progressive nature of the disease, most patients with type 2 diabetes inevitably proceed from oral agent monotherapy to combination therapy and, ultimately, require exogenous insulin replacement. Insulin therapy in type 2 diabetes is also accompanied by untoward **weight gain.** Both type 1 and type 2 diabetes continue to be characterized by marked postprandial hyperglycemia. Two hormones still in development are candidates for pharmacol. intervention, have novel modes of action (some centrally mediated), and show great promise in addressing some of the unmet needs of current diabetes management. Pramlintide acetate, an analog of the beta cell hormone amylin and the first non-insulin related therapeutic modality for type 1 and type 2 diabetic patients with severe beta cell failure, may be useful as adjunctive therapy to insulin. The principal anti-diabetic effects of pramlintide arise from interactions via its cognate receptors located in the central nervous system resulting in postprandial glucagon suppression, modulation of nutrient absorption rate, and reduction of food intake. Another polypeptide hormone, exendin-4, exerts at least some of its pharmacol. actions as an agonist at the glucagon-like peptide-1 (GLP-1) receptor. GLP-1 and related compds. exhibit multiple modes of action, the most notable being a glucose-dependent insulinotropic effects and the potential to preserve or improve the beta-cell function. The latter effect could potentially halt or delay the progressive deterioration of the diabetic state associated with type 2 diabetes. Physiol., both amylin and glucagon-like peptide (GLP)-1, along with insulin, are involved in a coordinated and concerted interplay between hormones acting both centrally and peripherally to provide meticulous control over the rate of appearance of exogenous and endogenous glucose and to match that rate to the rate of glucose disappearance. Both hormones are deficient in diabetes. Therapies directed at restoring this complex physiol. have the potential to facilitate glucose control and thus minimize the attendant complications of diabetes.

IT **187887-46-3**, Pramlintide acetate
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(novel peptides under development for treatment of type 1 and type 2 diabetes mellitus in humans)

REFERENCE COUNT: 169 THERE ARE 169 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 28 OF 35 CAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 23 Apr 2002
ACCESSION NUMBER: 2002:304437 CAPLUS
DOCUMENT NUMBER: 136:380428
TITLE: A randomized study and open-label extension evaluating the long-term efficacy of pramlintide as an adjunct to insulin therapy in type 1 diabetes
AUTHOR(S): Whitehouse, Fred; Kruger, Davida F.; Fineman, Mark; Shen, Larry; Ruggles, James A.; Maggs, David G.; Weyer, Christian; Kolterman, Orville G.
CORPORATE SOURCE: Henry Ford Hospital, Detroit, MI, USA
SOURCE: Diabetes Care (2002), 25(4), 724-730

CODEN: DICAD2; ISSN: 0149-5992
PUBLISHER: American Diabetes Association, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Aim was to assess the effect of mealtime amylin replacement with pramlintide on long-term glycemic and weight control in patients with type 1 diabetes. In a 52-wk, double-blind, placebo-controlled, multicenter study, 480 patients with type 1 diabetes were randomized to receive preprandial injections of placebo or 30 μg pramlintide q.i.d., in addition to existing insulin regimens. At week 20, pramlintide-treated patients were re-randomized to 30 or 60 μg pramlintide q.i.d. if decreases from baseline in HbA1c were <1% at week 13. Of the 342 patients who completed the 52-wk study, 236 individuals (.apprx.70%) elected to participate in a 1-yr open-label extension in which all patients received 30 or 60 μg pramlintide q.i.d.. Treatment with pramlintide led to a mean reduction in HbA1c of 0.67% from baseline to week 13 that was significantly ($P < 0.0001$) greater than the placebo reduction (0.16%), and a significant placebo-corrected treatment difference was sustained through week 52 ($P = 0.0071$). The greater HbA1c reduction was associated with an average weight loss, rather than **weight gain**, and was not accompanied by an increased overall event rate of severe hypoglycemia. In the open-label extension, mean HbA1c levels decreased rapidly in patients receiving pramlintide for the first time and remained at reduced levels in patients who continued pramlintide treatment. The most common adverse events reported by the pramlintide group were mild nausea and anorexia, which both occurred during the initial weeks of treatment and dissipated over time. Mealtime pramlintide treatment as an adjunct to insulin improved long-term glycemic control without inducing **weight gain** or increasing the overall risk of severe hypoglycemia in patients with type 1 diabetes.
IT **151126-32-8**, Pramlintide
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(efficacy of pramlintide, as an adjunct to insulin therapy, in type 1 diabetes)
REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 29 OF 35 CAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 19 Apr 2002
ACCESSION NUMBER: 2002:294239 CAPLUS
DOCUMENT NUMBER: 136:304085
TITLE: Method of treating the syndrome of coronary heart disease risk factors in humans using opiate antagonists, μ-opioids, and insulin secretagogues
INVENTOR(S): Clemens, Anton H.
PATENT ASSIGNEE(S): CPD, LLC, USA
SOURCE: U.S. Pat. Appl. Publ., 11 pp., Cont.-in-part of U.S. 6,262,062.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002045636	A1	20020418	US 2001-878834	20010611
US 6528520	B2	20030304		
US 6262062	B1	20010717	US 2000-639061	20000815
WO 2002100390	A2	20021219	WO 2002-US18863	20020606
WO 2002100390	A3	20040422		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2003036546	A1	20030220	US 2002-179993	20020625
US 6846831	B2	20050125		
US 2003149076	A1	20030807	US 2003-377838	20030303
US 6919310	B2	20050719		
US 2005250701	A1	20051110	US 2005-183059	20050715
PRIORITY APPLN. INFO.:			US 2000-639061	A2 20000815
			US 2001-878834	A 20010611
			US 2003-377838	A1 20030303

AB The invention provides an improved method of treating a human suffering from one or more conditions included within the Coronary Heart Disease Risk Factor (CHDRF) syndrome. The method includes administering, by a pharmaceutically effective mode, a drug composition having an opioidergic agent including an opiate antagonist, opiate having μ-agonist activity or combination thereof, and an insulin secretagogue. A 72-yr-old subject with type 2 diabetes and dyslipidemia was treated with hydrocodone in combination with glipizide.

IT **151126-32-8**, Pramlintide
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treating coronary heart disease risk factors syndrome in humans using opiate antagonists and μ-opioids and insulin secretagogues)

L3 ANSWER 30 OF 35 CAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 18 Jan 2002
ACCESSION NUMBER: 2002:51257 CAPLUS
DOCUMENT NUMBER: 136:123595
TITLE: A combination of phosphonate or phosphorodiamidate FBPase inhibitors and antidiabetic agents useful for the treatment of diabetes
INVENTOR(S): Van Poelje, Paul D.; Erion, Mark D.; Fujiwara, Toshihiko
PATENT ASSIGNEE(S): Metabasis Therapeutics, Inc., USA; Sankyo Company, Ltd.
SOURCE: PCT Int. Appl., 392 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1

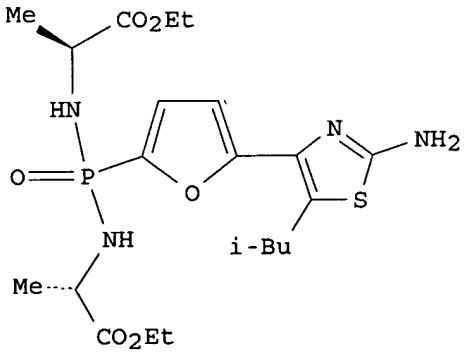
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002003978	A2	20020117	WO 2001-US21557	20010705
WO 2002003978	A3	20031016		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2412142	AA	20020117	CA 2001-2412142	20010705
US 2003073728	A1	20030417	US 2001-900364	20010705
BR 2001012212	A	20031230	BR 2001-12212	20010705
EP 1372660	A2	20040102	EP 2001-952530	20010705
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004508297	T2	20040318	JP 2002-508433	20010705
CN 1599612	A	20050323	CN 2001-814924	20010705
NZ 523227	A	20050429	NZ 2001-523227	20010705
ZA 2003000044	A	20040506	ZA 2003-44	20030102
NO 2003000034	A	20030305	NO 2003-34	20030103

PRIORITY APPLN. INFO.:	US 2000-216531P	P	20000706
	US 2001-900364	A	20010705
	US 2000-215126P	P	20000629
	WO 2001-US21557	W	20010705

OTHER SOURCE(S): MARPAT 136:123595

GI



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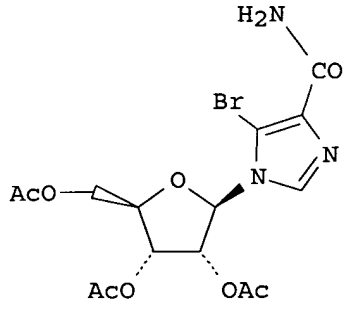

II

AB A combination therapy of at least one FBPase inhibitor ((R1Y)2P(O)M and R14C(O)(CR12R13)nN(R18)P(O)(NR15R16)M; e.g. 2-amino-5-propylthio-4-(5-phosphono-2-furanyl)thiazole monohydrobromide and 2-amino-5-isobutyl-4-[2-[N,N'-bis[(S)-1-(ethoxycarbonyl)ethyl]phosphonodiamido]-5-furanyl]thiazole (shown as I)) and at least one other

antidiabetic agent (insulin secretagogue; e.g. glyburide, a sulfonylurea) is disclosed. (R1Y)2P(O)M and R14C(O)(CR12R13)nN(R18)P(O)(NR15R16)M are converted in vivo or in vitro to MPO32-, which inhibit FBPase; the substituents are defined in the claims. General methods and about 15 specific example prepns. of the phosphorus compds. are included but no methods of preparation are claimed. In the biol. examples, data is presented for the following for selected phosphorus compds. and other materials: inhibition of human liver FBPase, inhibition of rat liver and mouse liver FBPase, inhibition of gluconeogenesis by an FBPase inhibitor in rat hepatocytes, inhibition of glucose production and elevation of fructose-1,6-bisphosphate levels in rat hepatocytes treated with FBPase inhibitors, anal. of hepatic and plasma drug metabolite levels, blood glucose, and hepatic fructose 1,6-bisphosphate levels after administration of compound A (shown as II) p.o. to normal fasted rats, anal. of hepatic and plasma drug levels after administration of compds. i.p. to normal fasted rats, oral bioavailability determination of two compds. and oral glucose lowering activity of two compds. For insulin secretagogues: insulin release from pancreatic islets, glucose lowering in the fasted rat, i.v. glucose tolerance in the fasted rat, oral glucose tolerance in the Zucker diabetic fatty rat, insulin secretion in the rat, inhibition of KATP-channels in mouse pancreatic beta-cells, and sulfonylurea receptor binding. Also included are: inhibition of dipeptidyl peptidase IV (DPP-IV inhibitors), alpha-glucosidase assay, glycogen phosphorylase assay, assay of glucose 6-phosphatase inhibitors, glucagon antagonist assay, amylin agonist assay, fatty acid oxidation inhibitor assay, glucose lowering in the db/db mouse (FBPase inhibitor), glucose lowering in the ZDF rat, acute combination treatment of an insulin secretagogue and an FBPase inhibitor in the ZDF rat, chronic combination treatment of an insulin secretagogue and an FBPase inhibitor in the ZDF rat, acute combination treatment of insulin and an FBPase inhibitor in db/db mice, beneficial effect of chronic combination treatment of insulin and an FBPase inhibitor in db/db mice, and beneficial effect of chronic combination treatment of insulin and an FBPase inhibitor in db/db Mice. Also included are: acute combination treatment of insulin and an FBPase inhibitor in the Goto-Kakizaki rat, acute combination treatment of a biguanide and an FBPase inhibitor in db/db mice, acute combination treatment of an alpha glucosidase inhibitor and an FBPase inhibitor in Goto-Kakizaki rats, acute combination treatment of a glycogen phosphorylase inhibitor and an FBPase inhibitor in db/db or ob/ob mice, acute combination treatment of a glucose-6-phosphatase inhibitor and an FBPase inhibitor in db/db or ob/ob mice, acute combination treatment of an FBPase inhibitor and an amylin agonist, chronic combination treatment of a fatty acid oxidation inhibitor and an FBPase inhibitor in the streptozotocin-induced diabetic rat.

IT **151126-32-8**, Pramlintide
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(amylin agonist; combination of phosphonate or phosphorodiamidate FBPase inhibitors and antidiabetic agents useful for treatment of diabetes)

L3 ANSWER 31 OF 35 CAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 18 Oct 2001
ACCESSION NUMBER: 2001:759575 CAPLUS
DOCUMENT NUMBER: 135:298797
TITLE: Synergistic effect of a sulfonylurea and/or non-sulfonylurea K+ ATP channel blocker, and a

phosphodiesterase 3 type inhibitor for the treatment of non-insulin-dependent diabetes or other conditions

INVENTOR(S): Fryburg, David Albert; Parker, Janice Catherine
PATENT ASSIGNEE(S): Pfizer Products Inc., USA

SOURCE: Eur. Pat. Appl., 19 pp.
CODEN: EPXXDW

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
EP 1145717	A2	20011017	EP 2001-303020		20010330
EP 1145717	A3	20020814			
EP 1145717	B1	20040512			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO					
AT 266409	E	20040515	AT 2001-303020		20010330
PT 1145717	T	20040831	PT 2001-303020		20010330
ES 2218338	T3	20041116	ES 2001-1303020		20010330
US 2002013268	A1	20020131	US 2001-829874		20010410
US 6610746	B2	20030826			
CA 2343850	AA	20011013	CA 2001-2343850		20010411
BR 2001001461	A	20011113	BR 2001-1461		20010411
JP 2001354568	A2	20011225	JP 2001-115674		20010413
US 2003216294	A1	20031120	US 2003-456371		20030605
PRIORITY APPLN. INFO.:			US 2000-196728P	P	20000413
			US 2001-829874	A3	20010410

AB The invention provides the use of a synergistic amount of (1) a sulfonylurea, a non-sulfonylurea K+ ATP channel blocker, or a sulfonylurea and a non-sulfonylurea K+ ATP channel blocker; and (2) a cAMP phosphodiesterase type 3 inhibitor; for the manufacture of medicaments for treating or preventing non-insulin-dependent diabetes mellitus, insulin resistance, Syndrome X, diabetic neuropathy, diabetic nephropathy, diabetic retinopathy, diabetic cardiomyopathy, polycystic ovary syndrome, cataracts, hyperglycemia, or impaired glucose tolerance. The invention also provides kits and pharmaceutical compns. that comprise (1) a sulfonylurea, a non-sulfonylurea K+ ATP channel blocker, or a sulfonylurea and a non-sulfonylurea K+ ATP channel blocker: and (2) a cAMP phosphodiesterase type 3 inhibitor. The invention further provides kits and pharmaceutical compns. that comprise (1) a sulfonylurea, a non-sulfonylurea K+ ATP channel blocker, or a sulfonylurea and a non-sulfonylurea K+ ATP channel blocker: (2) a cAMP phosphodiesterase type 3 inhibitor; and (3) an addnl. compound useful for the treatment of non-insulin-dependent diabetes mellitus, insulin resistance, Syndrome X, diabetic neuropathy, diabetic nephropathy, diabetic retinopathy, diabetic cardiomyopathy, polycystic ovary syndrome, cataracts, hyperglycemia, or impaired glucose tolerance.

IT **187887-46-3**, Symlin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(sulfonylurea and/or non-sulfonylurea K+ ATP channel blocker and phosphodiesterase 3 type inhibitor synergism for treatment of non-insulin-dependent diabetes or other conditions)

L3 ANSWER 32 OF 35 CAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 28 Sep 2001
ACCESSION NUMBER: 2001:709687 CAPLUS
DOCUMENT NUMBER: 135:272869
TITLE: Synthesis of indolyl-amides as glycogen phosphorylase inhibitors for treatment of type 2 diabetes
INVENTOR(S): Treadway, Judith Lee
PATENT ASSIGNEE(S): Pfizer Products Inc., USA
SOURCE: Eur. Pat. Appl., 78 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
EP 1136071	A2	20010926	EP 2001-301979		20010305
EP 1136071	A3	20030326			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO					
JP 2001302546	A2	20011031	JP 2001-78839		20010319
CA 2341344	AA	20010922	CA 2001-2341344		20010320
ZA 2001002318	A	20020920	ZA 2001-2318		20010320
US 2003004162	A1	20030102	US 2001-813335		20010320
NZ 510677	A	20021025	NZ 2001-510677		20010321
PRIORITY APPLN. INFO.:			US 2000-191381P	P	20000322

OTHER SOURCE(S): MARPAT 135:272869
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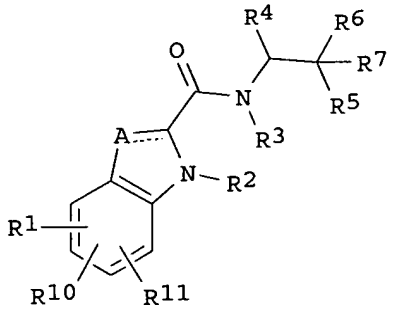

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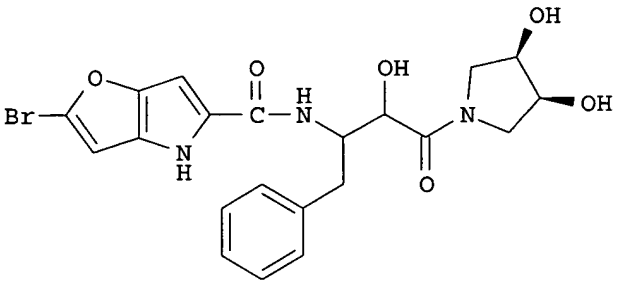

II

AB Title compds. I [A = CH, C-alkyl, C-halo when the dotted line is a bond; A = CH2, CH-alkyl when the dotted line is not a bond; R1, R10, R11 = H, halo, 4-, 6- or 7-NO2, CN, alkyl, alkoxy, (di/tri)fluoromethyl; R2 = H; R3 = H, alkyl; R4 = H, (hydroxy)alkyl, alkoxy-alkyl, phenyl(hydroxy)alkyl, thienyl-alkyl, etc.; R5 = H, OH, F, alkyl, alkoxy, alkanoyl, amino-alkoxy, etc.; R7 = H, F, alkyl; or R5 and R7 can be taken together to be oxo; R6 = carboxy, alkoxycarbonyl, amido, acyl, alkyl, OH, alkoxy; R9 = H, alkyl, OH, alkoxy, methyleneperfluorinated-alkyl, Ph, pyridyl, thienyl, etc.] and derivs. were prepared Over 50 examples were reported. For instance, 2-bromo-4H-furo[3,2-b]pyrrole-5-carboxylic acid was coupled to 2-amino-1-(3,4-dihydroxypyrrolidin-1-yl)-3-phenylpropan-1-one hydrochloride (DCM, DMF, HOBt, EDC, room temperature) to give amide II. Compds. I are glycogen phosphorylase inhibitors used for treating type 2 diabetes mellitus in cases which have not yet presented, but in which there is an increased risk of developing such condition. Combination therapies of I and non-glycogen phosphorylase inhibiting anti-diabetic agents are also claimed.

IT **151126-32-8**, Pramlintide **187887-46-3**, AC-137
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical in combination with; synthesis of indolyl-amides as glycogen phosphorylase inhibitors for treatment of type 2 diabetes)

L3 ANSWER 33 OF 35 CAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 28 Aug 2001
ACCESSION NUMBER: 2001:620285 CAPLUS
DOCUMENT NUMBER: 135:313698
TITLE: Amylin replacement with pramlintide as an adjunct to insulin therapy in type 1 and type 2 diabetes mellitus: a physiological approach toward improved metabolic control

AUTHOR(S): Weyer, C.; Maggs, D. G.; Young, A. A.; Kolterman, O. G.
CORPORATE SOURCE: Amylin Pharmaceuticals Inc., San Diego, CA, 92121, USA
SOURCE: Current Pharmaceutical Design (2001), 7(14), 1353-1373
CODEN: CPDEFP; ISSN: 1381-6128
PUBLISHER: Bentham Science Publishers
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with refs. Destruction and dysfunction of pancreatic beta-cells, resulting in absolute and relative insulin deficiency, represent key abnormalities in the pathogenesis of type 1 and type 2 diabetes, resp. Following the discovery of amylin, a second beta-cell hormone that is co-secreted with insulin in response to nutrient stimuli, it was realized that diabetes represents a state of bihormonal beta cell deficiency and that lack of amylin action may contribute to abnormal glucose homeostasis. Exptl. studies show that amylin acts as a neuroendocrine hormone that complements the effects of insulin in postprandial glucose regulation through several centrally mediated effects. These include a suppression of postprandial glucagon secretion and a vagus-mediated regulation of gastric emptying, thereby helping to control the influx of endogenous and exogenous glucose, resp. In animal studies, amylin has also been shown to **reduce** food intake and **body wt** ., consistent with an addnl. satiety effect. Pramlintide is a soluble, non-aggregating, injectable, synthetic analog of human amylin currently under development for the treatment of type 1 and insulin-using type 2 diabetes. Long-term clin. studies have consistently demonstrated that pre-prandial s.c. injections of pramlintide, in addition to the current insulin regimen, **reduce** HbA1c and **body weight** in type 1 and type 2 diabetic patients,' without an increase in insulin use or in the event rate of severe hypoglycemia. The most commonly observed side effects were gastrointestinal-related, mainly mild nausea, which typically occurred upon initiation of treatment and resolved within days or weeks. Amylin replacement with pramlintide as an adjunct to insulin therapy is a novel physiol. approach toward improved long-term glycemic and weight control in patients with type 1 and type 2 diabetes.

IT **151126-32-8**, Pramlintide
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(amylin replacement with pramlintide as adjunct to insulin therapy in type 1 and type 2 diabetes mellitus in relation to physiol. approach toward improved metabolic control)

REFERENCE COUNT: 123 THERE ARE 123 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 34 OF 35 CAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 23 Dec 1998
ACCESSION NUMBER: 1998:804202 CAPLUS
DOCUMENT NUMBER: 130:33501
TITLE: Methods for treating **obesity**
INVENTOR(S): Duft, Bradford J.; Kolterman, Orville
PATENT ASSIGNEE(S): Amylin Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 58 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 9855144	A1	19981210	WO 1998-US11753		19980605
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG					
US 2003026812	A1	20030206	US 1997-870762		19970606
AU 9878230	A1	19981221	AU 1998-78230		19980605
NZ 501451	A	20011026	NZ 1998-501451		19980605
RU 2207871	C2	20030710	RU 2000-100346		19980605
CZ 294983	B6	20050413	CZ 1999-4360		19980605
BR 9809951	A	20000801	BR 1998-9951		19980606
NO 9905996	A	20000207	NO 1999-5996		19991206
US 2004022807	A1	20040205	US 1999-445517		19991206
PRIORITY APPLN. INFO.:			US 1997-870762	A	19970606
			WO 1998-US11753	W	19980605

AB Methods for treating **obesity** are disclosed which comprise administration of a therapeutically effective amount of an amylin or an amylin agonist, e.g., pramlintide, alone or in conjunction with another **obesity** relief agent. Addnl., methods for reducing insulin-induced **weight gain** are disclosed which comprise administration of a therapeutically effective amount of an amylin or an amylin agonist.

IT **151126-32-8P**, Pramlintide
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(amylin treatment of **obesity** and prevention of insulin-induced **weight gain** in diabetes)

REFERENCE COUNT: 30 THERE ARE 30 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 35 OF 35 CAPLUS COPYRIGHT 2006 ACS on STN
ED Entered STN: 08 Mar 1997
ACCESSION NUMBER: 1997:151518 CAPLUS
DOCUMENT NUMBER: 126:153176
TITLE: Appetite regulating compositions
INVENTOR(S): Rink, Timothy J.; Young, Andrew A.; Beeley, Nigel R. A.; Prickett, Katheryn S.
PATENT ASSIGNEE(S): Amylin Pharmaceuticals, Inc., USA; Rink, Timothy J.; Young, Andrew A.; Beeley, Nigel R. A.; Prickett, Katheryn S.
SOURCE: PCT Int. Appl., 65 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 9640196	A1	19961219	WO 1996-US9937		19960606
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG					
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA					
US 5739106	A	19980414	US 1995-477727		19950607
ZA 9604673	A	19970212	ZA 1996-4673		19960605
CA 2223611	AA	19961219	CA 1996-2223611		19960606
AU 9659908	A1	19961230	AU 1996-59908		19960606
EP 844882	A1	19980603	EP 1996-917273		19960606
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI					
CN 1192689	A	19980909	CN 1996-196092		19960606
JP 11507637	T2	19990706	JP 1996-502098		19960606
PRIORITY APPLN. INFO.:			US 1995-477727	A	19950607
			WO 1996-US9937	W	19960606

OTHER SOURCE(S): MARPAT 126:153176

AB Compns. and methods for reducing food intake, **suppressing appetite** and controlling body weight are provided. Such compns. may include an amylin agonist and a CCK agonist or a hybrid peptide.

IT **151126-32-8**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(appetite regulating compns. containing an amylin agonist and a CCK agonist)

(FILE 'CAPLUS' ENTERED AT 12:14:08 ON 16 MAY 2006)
L5 1 SEA ABB=ON PLU=ON L2 AND CONTROL?(3A)((BODY OR BODILY)(W)(WT OR WEIGH?))
L6 0 SEA ABB=ON PLU=ON L5 NOT L3

FILE 'MEDLINE' ENTERED AT 12:15:09 ON 16 MAY 2006

FILE 'BIOSIS' ENTERED AT 12:15:09 ON 16 MAY 2006

FILE 'EMBASE' ENTERED AT 12:15:09 ON 16 MAY 2006

L7 386 S L2

L11 22 SEA ABB=ON PLU=ON L7 AND (TREAT? OR THERAP? OR PREVENT?)(5A)(ANTIOBES? OR OBESE OR OBESITY OR (WEIGH? OR WT)(3A)GAIN? OR APPETITE(3A)(DEPRESS? OR SUPPRESS?) OR ((BODY OR BODILY)(W)(WT OR WEIGH?))(3A)(REDUC? OR CONTROL?))
L12 19 DUP REM L11 (3 DUPLICATES REMOVED)

L12 ANSWER 1 OF 19 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 2006218954 MEDLINE
DOCUMENT NUMBER: PubMed ID: 16625817
TITLE: Obesity drugs in clinical development.
AUTHOR: Halford Jason C G

Searcher : Shears 571-272-2528

CORPORATE SOURCE: University of Liverpool, Kissileff Laboratory for the Study of Human Ingestive Behaviour, School of Psychology, Eleanor Rathbone Building, Bedford Street South, Liverpool, UK.. j.c.g.halford@liverpool.ac.uk
SOURCE: Current opinion in investigational drugs (London, England : 2000), (2006 Apr) Vol. 7, No. 4, pp. 312-8. Ref: 83
Journal code: 100965718. ISSN: 1472-4472.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200605
ENTRY DATE: Entered STN: 22 Apr 2006
Last Updated on STN: 6 May 2006
Entered Medline: 5 May 2006

AB A number of anti-obesity drugs are currently undergoing clinical development. These include: (i) centrally-acting drugs, such as the noradrenergic and dopaminergic reuptake inhibitor radafaxine, the endocannabinoid antagonist rimonabant, the selective serotonin 5-HT2c agonist APD-356, and oleoyl-estrone; (ii) drugs that target peripheral episodic satiety signals, such as glucagon-like peptide-1 (exenatide, exenatide-LAR and liraglutide), peptide YY (intranasal PYY3-36 and AC-162325) and amylin (pramlintide); (iii) drugs that block fat absorption, such as the novel lipase inhibitors cetilistat and GT-389255; and (iv) a human growth hormone fragment (AOD-9604) that increases adipose tissue breakdown. Of these, only rimonabant has got as far as completing phase III clinical trials. This review will provide an overview of the most prominent drugs currently undergoing clinical development as potential anti-**obesity therapies.**

L12 ANSWER 2 OF 19 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 2006139596 EMBASE
TITLE: Appetite regulatory peptides - Obesity drugs and their targets: Correlation of mouse knockout phenotypes with drug effects in vivo.
AUTHOR: Powell D.R.
CORPORATE SOURCE: D.R. Powell, Department of Endocrinology, Pharmaceutical Biology, Lexicon Genetics Incorporated, 8800 Technology Forest Place, The Woodlands, TX 77381-1160, United States. dpowell@lexgen.com
SOURCE: Obesity Reviews, (2006) Vol. 7, No. 1, pp. 89-108. .
Refs: 195
ISSN: 1467-7881 E-ISSN: 1467-789X CODEN: ORBEBL
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 003 Endocrinology
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 5 Apr 2006
Last Updated on STN: 5 Apr 2006

AB Sequencing of the human genome has yielded thousands of potential drug targets. The difficulty now is in determining which targets have real therapeutic value and should be the focus of a drug discovery effort.

The available evidence suggests that knockout technology can be used prospectively to identify targets that are amenable to drug development for the treatment of a variety of diseases. This review compares the knockout phenotypes of 21 potential **obesity** targets with the effects of **therapeutics** designed for those targets on rodents and, when data were available, on humans. The phenotypes of obesity target knockouts model the effects seen when **therapeutics** designed for those **obesity** targets are delivered to rodents; of the 21 obesity targets reviewed, 16 showed a correspondence between knockout phenotype and drug effect in mice and/or rats. This suggests that, at least in terms of evaluating obesity targets, it is rare for compensatory developmental changes caused by the gene knockout to prevent detection of the relevant phenotype. In the majority of cases, the knockout phenotypes also modelled the effects seen when the relevant therapeutics were delivered to humans. Thus, it seems rational to use mouse knockout technology prospectively to identify genes that regulate body fat in vivo, and then to develop anti-**obesity therapeutics** by targeting the human protein products of these genes. Ultimately, the value of using this approach to identify novel targets for human anti-**obesity therapies** will be judged by future studies examining the anti-**obesity** effect, in humans, of the **therapeutics** that result from this approach. .COPYRGT. 2006 The International Association for the Study of Obesity.

L12 ANSWER 3 OF 19 EMBASE

ACCESSION NUMBER: 2006125348 EMBASE

TITLE: The effect of hyperglycemia and its therapies on the heart.

AUTHOR: Wyne K.L.

CORPORATE SOURCE: Dr. K.L. Wyne, Division of Endocrinology and Metabolism, Department of Internal Medicine, University of Texas Southwestern Medical Center at Dallas, 5323 Harry Hines Boulevard, Dallas, TX 75390-8857, United States. Kathleen.Wyne@UTSouthwestern.edu

SOURCE: Heart Failure Clinics, (2006) Vol. 2, No. 1, pp. 61-70.
.
Refs: 58
ISSN: 1551-7136

PUBLISHER IDENT.: S 1551-7136(06)00005-5

COUNTRY: United States

DOCUMENT TYPE: Journal; General Review

FILE SEGMENT:
003 Endocrinology
018 Cardiovascular Diseases and Cardiovascular Surgery
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles

LANGUAGE: English

SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 31 Mar 2006
Last Updated on STN: 31 Mar 2006

AB Diabetes is a multiorgan disease. Therapy must now be targeted toward treating the underlying disease process and not just lowering the serum glucose level. Preventing the vascular disease and progression to heart failure has become an important goal of **therapy** as the epidemic of **obesity** and type 2 diabetes explodes. Heart failure is no longer limited to the geriatric population. With type 2 DM now being identified in youth and adolescents, heart failure will

soon be seen in people in their third and fourth decades. Therapies to control blood glucose must now target the lipotoxicity and the inflammation and optimize the AMPK system, in addition to lowering glucose, to prevent the epidemic of cardiac disease and heart failure that has been developing in recent years.

L12 ANSWER 4 OF 19 EMBASE

ACCESSION NUMBER: 2005379441 EMBASE
TITLE: Emerging drugs for obesity: Linking novel biological mechanisms to pharmaceutical pipelines.
AUTHOR: Correia M.L.G.; Haynes W.G.
CORPORATE SOURCE: Dr. M.L.G. Correia, University of Iowa, Department of Internal Medicine, Carver College of Medicine, Iowa City, IA 52242, United States. marcelo-correia@uiowa.edu
SOURCE: Expert Opinion on Emerging Drugs, (2005) Vol. 10, No. 3, pp. 643-660. .
Refs: 82
ISSN: 1472-8214 CODEN: EOEDA3
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 003 Endocrinology
006 Internal Medicine
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 22 Sep 2005
Last Updated on STN: 22 Sep 2005

AB Obesity is associated with hypertension, diabetes, dyslipidaemias and metabolic syndrome, and causes substantial morbidity and mortality from cardiovascular and other diseases. The cost to **treat obesity** and its complications in the US has increased steeply and is currently estimated to be US$100 billion. Current **therapy** for **obesity** is mainly based on changes in lifestyle that often fail. Existing pharmacological treatment is marginally efficient and poorly tolerated. The discovery of leptin and related neural mechanisms of energy metabolism regulation has opened the doors to potential targets for new antiobesity drugs. In this review, new pharmacological targets are discussed and an update on the development of emerging antiobesity drugs is provided. Despite intense investigation, the pipelines for antiobesity drugs in late stages of development are relatively empty. Breakthrough **treatments** for **obesity** may take some years to emerge. Clinical trials will be necessary to clarify the impact of new antiobesity drugs on hard cardiovascular and metabolic end points. .COPYRGT. 2005 Ashley Publications Ltd.

L12 ANSWER 5 OF 19 EMBASE

ACCESSION NUMBER: 2005509303 EMBASE
TITLE: Drugs on the horizon for diabesity.
AUTHOR: Bailey C.J.
CORPORATE SOURCE: Dr. C.J. Bailey, Diabetes Group, Department of Life and Health Sciences, Aston University, Aston Triangle, Birmingham B4 7ET, United Kingdom. c.j.bailey@aston.ac.uk
SOURCE: Current Diabetes Reports, (2005) Vol. 5, No. 5, pp.

353-359. .
Refs: 72
ISSN: 1534-4827 CODEN: CDRUAK
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 003 Endocrinology
006 Internal Medicine
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 1 Dec 2005
Last Updated on STN: 1 Dec 2005

AB The coexistence of type 2 diabetes and **obesity** presents a complex **therapeutic** challenge. Future combination tablets may include agents to address diabetes and any accompanying cardiovascular risk factors. Injectable agents that improve glycemic control and facilitate weight loss have recently become available: the soluble amylin analogue pramlintide provides an adjunct to insulin therapy in type 1 and type 2 diabetes, and the incretin mimetic exenatide can enhance prandial insulin release in type 2 diabetes. Orally active inhibitors of the incretin-degrading enzyme dipeptidyl peptidase-IV, agonists of peroxisome proliferator-activated receptor (PPAR)-α and PPAR-γ ("dual PPARs"), and the CBI cannabinoid receptor inhibitor rimonabant are advanced in clinical development. Many novel antidiabetic and antiobesity compounds are emerging in preclinical development. Copyright .COPYRGT. 2005 by Current Science Inc.

L12 ANSWER 6 OF 19 EMBASE

ACCESSION NUMBER: 2006134632 EMBASE
TITLE: The gastrointestinal tract and the regulation of appetite.
AUTHOR: Chaudhri O.B.; Small C.J.; Bloom S.R.
CORPORATE SOURCE: S.R. Bloom, Department of Metabolic Medicine, Hammersmith Hospital, Imperial College London, London W12 0NN, United Kingdom. s.bloom@imperial.ac.uk
SOURCE: Drug Discovery Today: Disease Mechanisms, (2005) Vol. 2, No. 3, pp. 289-294. .
Refs: 47
ISSN: 1740-6765
PUBLISHER IDENT.: S 1740-6765(05)00067-2
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 003 Endocrinology
005 General Pathology and Pathological Anatomy
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
048 Gastroenterology
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 3 Apr 2006
Last Updated on STN: 3 Apr 2006

AB The increasing incidence of obesity worldwide has renewed interest in the control of food intake and energy homeostasis. The brain-gut axis is central to the mechanism by which the periphery signals energy status to central nervous appetite centres. Gut hormones such as

peptide YY, glucagon-like peptide-1 and oxyntomodulin induce satiety and reduce food intake, whereas ghrelin is the hormone of hunger, and promotes feeding. Manipulation of the brain-gut axis offers an attractive strategy for the development of an effective medical **therapy** for **obesity.** .COPYRGT. 2005 Elsevier Ltd.

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ACCESSION NUMBER: 2005134230 EMBASE
TITLE: The hypothalamus and obesity.
AUTHOR: King P.J.
CORPORATE SOURCE: P.J. King, J/J Pharmaceutical Research/Devmt., A Div. of Janssen Pharmaceutic N.V., Department of Metabolic Disorders, Turnhoutseweg 30, B-2340 Beerse, Belgium. pking3@prdbe.jnj.com
SOURCE: Current Drug Targets, (2005) Vol. 6, No. 2, pp. 225-240. .
Refs: 266
ISSN: 1389-4501 CODEN: CDTUAU
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 003 Endocrinology
006 Internal Medicine
029 Clinical Biochemistry
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 7 Apr 2005
Last Updated on STN: 7 Apr 2005

AB Obesity, a condition already at epidemic proportions in the developed world, is largely attributable to an indulgent lifestyle. Biologically we feel hunger more acutely than feeling 'full-up' (satiety). The discovery over a decade ago of leptin, an adiposity signal, revolutionised our understanding of hypothalamic mechanisms underpinning the central control of ingestive behaviour. The structure and function of many hypothalamic peptides (Neuropeptide Y (NPY), Melanocortins, Agouti related peptide (AGRP), Cocaine and amphetamine regulated transcript (CART), Melanin concentrating hormone (MCH), Orexins and endocannabinoids) have been characterised in rodent models. The pharmacological potential of several endogenous peripheral peptides released prior to, during and/or after feeding are being explored. Short-term signal hormones including Cholecystokinin (CCK), Ghrelin, Peptide YY (PYY(3-36)) and Glucagon-like peptide 1 (GLP-1) control meal size via pathways converging on the hypothalamus. Long-term regulation is provided by the main circulating hormones leptin and insulin. These systems among others, implicated in hypothalamic appetite regulation all provide potential "drugable" targets by which to **treat obesity.** .COPYRGT. 2005 Bentham Science Publishers Ltd.

L12 ANSWER 8 OF 19 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2005251335 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15891954
TITLE: Adjunctive therapy with pramlintide lowers HbA1c without concomitant weight gain and increased risk of severe hypoglycemia in patients with type 1 diabetes approaching glycemic targets.

AUTHOR: Ratner R; Whitehouse F; Fineman M S; Strobel S; Shen L; Maggs D G; Kolterman O G; Weyer C
CORPORATE SOURCE: MedStar Clinical Research Institute, Washington, DC, USA.
SOURCE: Experimental and clinical endocrinology & diabetes : official journal, German Society of Endocrinology [and] German Diabetes Association, (2005 Apr) Vol. 113, No. 4, pp. 199-204.
Journal code: 9505926. ISSN: 0947-7349.
PUB. COUNTRY: Germany: Germany, Federal Republic of
DOCUMENT TYPE: (CLINICAL TRIAL)
(CONTROLLED CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200509
ENTRY DATE: Entered STN: 14 May 2005
Last Updated on STN: 27 Sep 2005
Entered Medline: 26 Sep 2005

AB AIMS: In long-term clinical trials in patients with type 1 diabetes spanning a wide range of HbA1c, addition of pramlintide to existing insulin regimens led to reductions in HbA1c that were accompanied by weight loss and no increase in overall severe hypoglycemia event rates. Given that weight gain and increased hypoglycemia risk contribute to the difficulty of attaining HbA1c targets (<7 %), the question arose whether pramlintide could benefit patients approaching, but not reaching glycemic targets with insulin alone. To address this question, we conducted a pooled analysis from 3 long-term clinical trials, including all patients with an entry HbA1c between 7.0 % and 8.5 %. METHODS: Within the subset of patients with an entry HbA1c between 7.0 % and 8.5 % (approximately 28 % of all patients enrolled in the 3 studies), 196 were treated with placebo + insulin (baseline HbA1c 7.9+/-0.4 %, body weight 76.0+/-14.3 kg [mean+/-SD]) and 281 with pramlintide+insulin (baseline HbA1c 7.9+/-0.4 %, body weight 75.4+/-13.1 kg). Endpoints included placebo-corrected changes from baseline to week 26 in HbA1c, body weight, and the event rate of severe hypoglycemia. RESULTS: Adjunctive **therapy** with pramlintide resulted in significant **reductions** in HbA1c and **body weight** from baseline to week 26 (0.3 % and 1.8 kg, placebo-corrected treatment differences, respectively, both p<or=0.0009). These changes occurred without an increase in the overall risk of severe hypoglycemia (1.40 pramlintide vs. 1.86 placebo, events/patient-year of exposure). CONCLUSIONS: Addition of pramlintide to insulin therapy may help patients with type 1 diabetes who are approaching, but not yet reaching, glycemic targets with insulin alone to achieve further reductions in HbA1c without concomitant weight gain and increased risk of severe hypoglycemia.

L12 ANSWER 9 OF 19 MEDLINE on STN
ACCESSION NUMBER: 2004197929 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15090634
TITLE: Effect of pramlintide on weight in overweight and **obese** insulin-**treated** type 2 diabetes patients.
AUTHOR: Hollander Priscilla; Maggs David G; Ruggles James A; Fineman Mark; Shen Larry; Kolterman Orville G; Weyer Christian
CORPORATE SOURCE: Baylor College of Medicine, Dallas, Texas, USA.
SOURCE: Obesity research, (2004 Apr) Vol. 12, No. 4, pp. 661-8.
Journal code: 9305691. ISSN: 1071-7323.

PUB. COUNTRY: United States
DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200407
ENTRY DATE: Entered STN: 20 Apr 2004
Last Updated on STN: 17 Jul 2004
Entered Medline: 16 Jul 2004

AB OBJECTIVE: Several randomized, placebo-controlled, double-blind trials in insulin-treated patients with type 2 diabetes have shown that adjunctive therapy with pramlintide reduces hemoglobin (Hb)A1c with concomitant weight loss. This analysis further characterizes the weight-lowering effect of pramlintide in this patient population. RESEARCH METHODS AND PROCEDURES: This pooled post hoc analysis of two long-term trials included all patients who were overweight/obese at baseline (BMI > 25 kg/m2), and who were treated with either 120 microg pramlintide BID (n = 254; HbA1c 9.2%; weight, 96.1 kg) or placebo (n = 244; HbA1c 9.4%; weight, 95.0 kg). Statistical endpoints included changes from baseline to week 26 in HbA1c, body weight, and insulin use. RESULTS: Pramlintide treatment resulted in significant reductions from baseline to week 26, compared with placebo, in HbA1c and body weight (both, $p < 0.0001$), for placebo-corrected reductions of -0.41% and -1.8 kg, respectively. Approximately three times the number of patients using pramlintide experienced a > or = 5% reduction of body weight than with placebo (9% vs. 3%, $p = 0.0005$). Patients using pramlintide also experienced a proportionate decrease in total daily insulin use ($r = 0.39$, $p < 0.0001$). The greatest placebo-corrected reductions in weight at week 26 were observed in pramlintide-treated patients with a BMI >40 kg/m2 and in those concomitantly treated with metformin (both, $p < 0.001$), for placebo-corrected reductions of -3.2 kg and -2.5 kg, respectively. DISCUSSION: These findings support further evaluation of the weight-lowering potential of pramlintide in obese patients with type 2 diabetes.

L12 ANSWER 10 OF 19 EMBASE
ACCESSION NUMBER: 2004390609 EMBASE
TITLE: **Weight gain** and insulin **therapy.**
AUTHOR: Khan R.
CORPORATE SOURCE: Dr. R. Khan, Basildon Hospital, Nethermayne, Basildon, Essex SS16 5NL, United Kingdom.
dr_rehman_khan@hotmail.com
SOURCE: British Journal of Diabetes and Vascular Disease, (2004) Vol. 4, No. 4, pp. 264-267. .
Refs: 30
ISSN: 1474-6514 CODEN: BJDVAI
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 003 Endocrinology
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 30 Sep 2004
Last Updated on STN: 30 Sep 2004

Searcher : Shears 571-272-2528

AB **Weight gain** is common with insulin **therapy** in type 1 and type 2 diabetes. Excessive weight gain worsens glycaemic control and increases cardiovascular risk. It can also increase diabetic morbidity and mortality if it acts as a psychological barrier to initiation or intensification of insulin therapy, or affects compliance. Insulin-associated weight gain might result from conservation of previously excreted glucose, defensive 'snacking' caused by fear or experience of hypoglycaemia, or the 'unphysiological' pharmacokinetic profiles that follow sc insulin administration. Strategies to limit insulin-mediated weight gain include increasing insulin sensitivity through dietary modification, exercise or insulin sensitising drugs. Attempts to replace insulin using regimens that accurately mimic physiological norms should also enable insulin to be dosed with maximum efficiency. The novel analogue insulin, detemir, has not shown the usual propensity for weight gain. Elucidation of the pharmacological mechanisms underlying this property could further clarify mechanisms linking insulin with weight regulation.

L12 ANSWER 11 OF 19 EMBASE

ACCESSION NUMBER: 2005484993 EMBASE
TITLE: Advances in diabetes for the millennium: Nutritional therapy of type 2 diabetes CME.
AUTHOR: Rendell M.
CORPORATE SOURCE: Dr. M. Rendell, Department of Medicine, Creighton University Diabetes Center, Omaha, NE, United States
SOURCE: MedGenMed Medscape General Medicine, (2004) Vol. 6, No. 3 SUPPL., pp. 8p. .
Refs: 40
CODEN: MMGMCE
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 003 Endocrinology
017 Public Health, Social Medicine and Epidemiology
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 17 Nov 2005
Last Updated on STN: 17 Nov 2005

AB Dietary modification is useful in both type 1 and type 2 diabetes. Glucose levels after a meal are largely determined by carbohydrate intake. Decreased intake of simple carbohydrates and increased fiber consumption lower postprandial glucose. Obesity has become epidemic in the United States and has dramatically increased the incidence of type 2 diabetes by augmenting insulin resistance. Dietary **treatment** of **obesity** has been frustrating. Success will require education in using foods with high fiber contents, low glycemic indexes, and low saturated fat levels. The use of natural foods must be supplemented by the use of semisynthetic foods with desirable properties. The educational efforts required are substantial and must be recognized by third-party reimbursement agencies. Operative procedures to decrease intake or reduce the absorption of food are being used with increasing frequency. Bariatric surgery is often successful in inducing a substantial loss of weight; however, this success must be balanced against the complications of surgery, which can be considerable. The pharmacologic approaches to **treatment** of **obesity**

have focused primarily on anorexigenic agents. Several polypeptides that induce satiety are currently under study, including leptin and glucagon-like peptide-1 (GLP-1). Orlistat has been used to induce the malabsorption of fat to reduce caloric ingestion. Of the currently used oral hypoglycemics, metformin and the disaccharidase inhibitors have the best tendency to promote weight loss. There is active research on the uncoupling proteins that induce thermogenesis and promote the dissipation of calories. The beta-3 agonists act through the uncoupling proteins. The thiazolidinediones tend to promote weight gain through the PPAR gene locus. Agents that antagonize this effect could induce weight loss. The future will undoubtedly bring us drugs that are effective in causing weight loss. The advent of drugs to successfully combat obesity will substantially improve public health. .COPYRGT. 2004 Medscape.

L12 ANSWER 12 OF 19 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 2003:531259 BIOSIS
DOCUMENT NUMBER: PREV200300531288
TITLE: The human amylin analog, pramlintide, **reduces body weight** in insulin-**treated** patients with type 2 diabetes.
AUTHOR(S): Weyer, C. [Reprint Author]; Maggs, D. [Reprint Author]; Ruggles, J. [Reprint Author]; Fineman, M. [Reprint Author]; Burrell, T. [Reprint Author]; Kolterman, O. [Reprint Author]
CORPORATE SOURCE: Amylin Pharmaceuticals, Inc., San Diego, CA, USA
SOURCE: Diabetologia, (August 2003) Vol. 46, No. Supplement 2, pp. A 295. print.
Meeting Info.: 18th Congress of the International Diabetes Federation. Paris, France. August 24-29, 2003. International Diabetes Federation.
CODEN: DBTGAJ. ISSN: 0012-186X.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 12 Nov 2003
Last Updated on STN: 12 Nov 2003

L12 ANSWER 13 OF 19 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 2002:503790 BIOSIS
DOCUMENT NUMBER: PREV200200503790
TITLE: The human amylin analog, pramlintide, **reduces body weight** in insulin-**treated** patients with type 2 diabetes.
AUTHOR(S): Weyer, C. [Reprint author]; Maggs, D. G. [Reprint author]; Fineman, M. S. [Reprint author]; Burrell, T. [Reprint author]; Kolterman, O. G. [Reprint author]
CORPORATE SOURCE: Amylin Pharmaceuticals Inc., San Diego, CA, USA
SOURCE: International Journal of Obesity, (August, 2002) Vol. 26, No. Supplement 1, pp. S135. print.
Meeting Info.: Ninth International Congress on Obesity. Sao Paulo, Brazil. August 24-29, 2002.
CODEN: IJOBDP. ISSN: 0307-0565.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 25 Sep 2002
Last Updated on STN: 25 Sep 2002

Searcher : Shears 571-272-2528

L12 ANSWER 14 OF 19 MEDLINE on STN
ACCESSION NUMBER: 2002714950 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12477297
TITLE: Novel peptides under development for the treatment of type 1 and type 2 diabetes mellitus.
AUTHOR: Baron Alain D; Kim Dennis; Weyer Christian
CORPORATE SOURCE: Amylin Pharmaceuticals, Inc., 9373 Towne Centre Drive, Suite 250, San Diego, CA 92121, USA.. abaron@amylin.com
SOURCE: Current drug targets. Immune, endocrine and metabolic disorders, (2002 Apr) Vol. 2, No. 1, pp. 63-82. Ref: 169
Journal code: 101121150. ISSN: 1568-0088.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200301
ENTRY DATE: Entered STN: 17 Dec 2002
Last Updated on STN: 29 Jan 2003
Entered Medline: 28 Jan 2003

AB Recent availability of expanded treatment options for both type 1 and type 2 diabetes has not translated into easier and significantly better glycemic and metabolic management. Patients with type 1 diabetes continue to experience increased risk of hypoglycemic episodes and progressive **weight gain** resulting from intensive insulin **treatment**, despite the recent availability of a variety of insulin analog. Given the progressive nature of the disease, most patients with type 2 diabetes inevitably proceed from oral agent monotherapy to combination therapy and, ultimately, require exogenous insulin replacement. Insulin therapy in type 2 diabetes is also accompanied by untoward weight gain. Both type 1 and type 2 diabetes continue to be characterized by marked postprandial hyperglycemia. Two hormones still in development are candidates for pharmacologic intervention, have novel modes of action (some centrally mediated), and show great promise in addressing some of the unmet needs of current diabetes management. Pramlintide acetate, an analog of the beta cell hormone amylin and the first non-insulin related therapeutic modality for type 1 and type 2 diabetic patients with severe beta cell failure, may be useful as adjunctive therapy to insulin. The principal anti-diabetic effects of pramlintide arise from interactions via its cognate receptors located in the central nervous system resulting in postprandial glucagon suppression, modulation of nutrient absorption rate, and reduction of food intake. Another polypeptide hormone, exendin-4, exerts at least some of its pharmacologic actions as an agonist at the glucagon-like peptide-1 (GLP-1) receptor. GLP-1 and related compounds exhibit multiple modes of action, the most notable being a glucose-dependent insulinotropic effects and the potential to preserve or improve the beta-cell function. The latter effect could potentially halt or delay the progressive deterioration of the diabetic state associated with type 2 diabetes. Physiologically, both amylin and glucagon-like peptide (GLP)-1, along with insulin, are involved in a coordinated and concerted interplay between hormones acting both centrally and peripherally to provide meticulous control over the rate of appearance of exogenous and endogenous glucose and to match that rate to the rate of glucose disappearance. Both hormones are deficient in diabetes. Therapies directed at restoring this complex physiology have the potential to facilitate glucose control and thus minimize the

attendant complications of diabetes.

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ACCESSION NUMBER: 2002:568942 BIOSIS
DOCUMENT NUMBER: PREV200200568942
TITLE: Amylin replacement with pramlintide as an adjunct to insulin therapy facilitates a combined improvement in glycemic and weight control in type 1 diabetes.
AUTHOR(S): Weyer, C. [Reprint author]; Maggs, D. G. [Reprint author]; Fineman, M. [Reprint author]; Gottlieb, A. D. [Reprint author]; Shen, L. Z. [Reprint author]; Kolterman, O. G. [Reprint author]
CORPORATE SOURCE: Amylin Pharmaceuticals, Inc., 9373 Towne Centre Drive, San Diego, CA, 92121, USA
SOURCE: Diabetologia, (August, 2001) Vol. 44, No. Supplement 1, pp. A237. print.
Meeting Info.: 37th Annual Meeting of the European Association for the Study of Diabetes. Glasgow, Scotland, UK. September 09-13, 2001. European Association for the Study of Diabetes.
CODEN: DBTGAJ. ISSN: 0012-186X.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 7 Nov 2002
Last Updated on STN: 7 Nov 2002

L12 ANSWER 16 OF 19 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 2002:568941 BIOSIS
DOCUMENT NUMBER: PREV200200568941
TITLE: Amylin replacement with pramlintide as an adjunct to insulin therapy facilitates a combined improvement in glycemic and weight control in type 2 diabetes.
AUTHOR(S): Maggs, D. G. [Reprint author]; Weyer, C. [Reprint author]; Burrell, T. [Reprint author]; Gottlieb, A. D. [Reprint author]; Shen, L. Z. [Reprint author]; Kolterman, O. G. [Reprint author]
CORPORATE SOURCE: Amylin Pharmaceuticals, Inc., 9373 Towne Centre Drive, San Diego, CA, 92121, USA
SOURCE: Diabetologia, (August, 2001) Vol. 44, No. Supplement 1, pp. A237. print.
Meeting Info.: 37th Annual Meeting of the European Association for the Study of Diabetes. Glasgow, Scotland, UK. September 09-13, 2001. European Association for the Study of Diabetes.
CODEN: DBTGAJ. ISSN: 0012-186X.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 7 Nov 2002
Last Updated on STN: 7 Nov 2002

L12 ANSWER 17 OF 19 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2001225033 EMBASE
TITLE: **Obesity**: Causes and new **treatments.**
AUTHOR: Lefebvre P.L.; Scheen A.J.
CORPORATE SOURCE: Dr. P.L. Lefebvre, Metabolic Disorders Unit, C.H.U.

Sart Tilman, B-4000 Liege 1, Belgium
SOURCE: Experimental and Clinical Endocrinology and Diabetes, (2001) Vol. 109, No. SUPPL. 2, pp. S215-S224. .
Refs: 53
ISSN: 0947-7349 CODEN: ECEDFQ
COUNTRY: Germany
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 003 Endocrinology
009 Surgery
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 19 Jul 2001
Last Updated on STN: 19 Jul 2001

AB The prevalence of obesity increases rapidly in developed and developing countries. Obesity results from a cumulative positive energy balance and is favoured by both genetic and environmental factors. **Preventing obesity** requires a major investment in nutritional and lifestyle education, particularly in children and adolescents. - The pharmacological approach to obesity includes drugs that reduce food intake (noradrenergic and serotoninergic agents), drugs that increase energy expenditure and compounds that affect nutrient partitioning. In all instances, the benefit-to-risk ratio needs to be carefully assessed. In some patients (severe obesity or obesity accompanied by serious high-risk comorbid conditions), gastric surgery (gastric restriction or gastric bypass) should be considered. In our own experience, it is safe and effective.

L12 ANSWER 18 OF 19 EMBASE

ACCESSION NUMBER: 2000236494 EMBASE
TITLE: 9th International Conference on Obesity, NIDDM, Adipogenesis and Insulin Resistance, London, UK, 3-5 April 2000.
AUTHOR: Wang S.
CORPORATE SOURCE: S. Wang, Schering-Plough Res. Institute, K15-C331-3600, 2015 Galloping Hill Road, Kenilworth, NJ 07033, United States. suke.wang@spcorp.com
SOURCE: Expert Opinion on Investigational Drugs, (2000) Vol. 9, No. 7, pp. 1673-1678. .
Refs: 0
ISSN: 1354-3784 CODEN: EOIDER
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 006 Internal Medicine
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20 Jul 2000
Last Updated on STN: 20 Jul 2000

AB The 9th International Conference on Obesity, NIDDM, Adipogenesis and Insulin Resistance was held between 3rd and 5th April, 2000 in London, UK. The three day conference was attended by more than 100 delegates from both academic and industrial institutions. Conference topics covered the use of genetics in obesity and diabetes, etiology and implications of **treatment** for **obesity**, progress in identification of new obesity and Type 2 diabetes drug targets, islet cell targets, progress in drugs for insulin enhancement and

sensitisation, adipogenesis and insulin resistance. Below are meeting highlights closely related to new drug developments and drug target identification in these therapeutic areas.

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ACCESSION NUMBER: 97239658 EMBASE
DOCUMENT NUMBER: 1997239658
TITLE: Oncologic, Endocrine and Metabolic. 57th American Diabetes Association Annual Meeting.
AUTHOR: Colca J.
CORPORATE SOURCE: J. Colca, Endocrine Pharm. and Metabolism, Pharmacia and Upjohn, Inc., 301 Henrietta St., Kalamazoo, MI 49007-0199, United States
SOURCE: Expert Opinion on Investigational Drugs, (1997) Vol. 6, No. 8, pp. 1113-1115. .
Refs: 7
ISSN: 1354-3784 CODEN: EOIDER
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 003 Endocrinology
006 Internal Medicine
029 Clinical Biochemistry
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 4 Sep 1997
Last Updated on STN: 4 Sep 1997

AB The annual meeting of the American Diabetes Association was held in Boston, MA. There were over 6500 participants, one-third from overseas, and 1103 papers were presented. Abstracts from the meeting have been published [1], from which abstract numbers are given below, e.g., (A141). Considerable progress has been made in understanding the complexities of diabetes and **obesity**, and new **treatments** for diabetes and associated metabolic diseases have great potential. These are likely to expand greatly by the further elucidation of specific metabolic defects that exist, improved diagnosis of the existing disease, as well as the development of novel or as yet under-utilised-drugs.

FILE 'HOME' ENTERED AT 12:18:54 ON 16 MAY 2006

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=> d his ful

     (FILE 'HOME' ENTERED AT 12:07:42 ON 16 MAY 2006)
               SET COST OFF

     FILE 'REGISTRY' ENTERED AT 12:07:50 ON 16 MAY 2006
L1            14 SEA ABB=ON  PLU=ON  KCNTATCATQRLANFLVHSSNNFGPILPPTNVGSNTY/S
               QSP

     FILE 'REGISTRY' ENTERED AT 12:08:22 ON 16 MAY 2006
               D QUE
               D 1-14 .BEVREG1

     FILE 'CAPLUS' ENTERED AT 12:08:27 ON 16 MAY 2006
L2           111 SEA ABB=ON  PLU=ON  L1
L3            35 SEA ABB=ON  PLU=ON  L2 AND (ANTIOBES? OR OBESE OR OBESITY
               OR (WEIGH? OR WT)(3A)GAIN? OR APPETITE(3A)(DEPRESS? OR
               SUPPRESS?) OR ((BODY OR BODILY)(W)(WT OR WEIGH?))(3A)REDUC?
               )
L*** DEL       6 S L2(L)(ANTIOBES? OR OBESE OR OBESITY OR (WEIGH? OR WT)(3A)
L*** DEL       1 S L4 AND DUFT ?/AU
               D KWIC
               D 1-35 .BEVSTR

     FILE 'MEDLINE, BIOSIS, EMBASE' ENTERED AT 12:13:26 ON 16 MAY 2006
L4           386 SEA ABB=ON  PLU=ON  L1

     FILE 'CAPLUS' ENTERED AT 12:14:08 ON 16 MAY 2006
L5             1 SEA ABB=ON  PLU=ON  L2 AND CONTROL?(3A)((BODY OR BODILY)(W)
               (WT OR WEIGH?))
L6             0 SEA ABB=ON  PLU=ON  L5 NOT L3

     FILE 'MEDLINE, BIOSIS, EMBASE' ENTERED AT 12:15:09 ON 16 MAY 2006
L7           386 SEA ABB=ON  PLU=ON  L2
L8             0 SEA ABB=ON  PLU=ON  L7(L)(ANTIOBES? OR OBESE OR OBESITY OR
               (WEIGH? OR WT)(3A) GAIN? OR APPETITE(3A)(DEPRESS? OR
               SUPPRESS?) OR ((BODY OR BODILY)(W)(WT OR WEIGH?))(3A)(REDUC
               ? OR CONTROL?))
L9            42 SEA ABB=ON  PLU=ON  L7 AND (TREAT? OR THERAP? OR PREVENT?)(
               S)(ANTIOBES? OR OBESE OR OBESITY OR (WEIGH? OR WT)(3A)
               GAIN? OR APPETITE(3A)(DEPRESS? OR SUPPRESS?) OR ((BODY OR
               BODILY)(W)(WT OR WEIGH?))(3A)(REDUC? OR CONTROL?))
L10           32 DUP REM L9 (10 DUPLICATES REMOVED)
               D KWIC
               D KWIC 3
L11           22 SEA ABB=ON  PLU=ON  L7 AND (TREAT? OR THERAP? OR PREVENT?)(
               5A)(ANTIOBES? OR OBESE OR OBESITY OR (WEIGH? OR WT)(3A)
               GAIN? OR APPETITE(3A)(DEPRESS? OR SUPPRESS?) OR ((BODY OR
               BODILY)(W)(WT OR WEIGH?))(3A)(REDUC? OR CONTROL?))
L12           19 DUP REM L11 (3 DUPLICATES REMOVED)
               D 1-19 IBIB ABS

     FILE 'HOME' ENTERED AT 12:18:54 ON 16 MAY 2006


     FILE HOME

     FILE REGISTRY
     Property values tagged with IC are from the ZIC/VINITI data file
     provided by InfoChem.
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STRUCTURE FILE UPDATES: 15 MAY 2006 HIGHEST RN 884382-45-0
DICTIONARY FILE UPDATES: 15 MAY 2006 HIGHEST RN 884382-45-0

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH January 6, 2006

Please note that search-term pricing does apply when conducting SmartSELECT searches.

****
* *
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added, *
* effective March 20, 2005. A new display format, IDERL, is now *
* available and contains the CA role and document type information. *
* *
****

Structure search iteration limits have been increased. See HELP SLIMI for details.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

http://www.cas.org/ONLINE/UG/regprops.html

FILE CAPLUS

FILE COVERS 1907 - 16 May 2006 VOL 144 ISS 21
FILE LAST UPDATED: 15 May 2006 (20060515/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply They are available for your review at:

http://www.cas.org/infopolicy.html

FILE MEDLINE
FILE LAST UPDATED: 13 MAY 2006 (20060513/UP). FILE COVERS 1950 TO DA

On December 11, 2005, the 2006 MeSH terms were loaded.

The MEDLINE reload for 2006 is now (26 Feb.) available. For details on the 2006 reload, enter HELP RLOAD at an arrow prompt (=>).
See also:

http://www.nlm.nih.gov/mesh/

http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html
http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_med_data_changes.ht
http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_2006_MeSH.html

OLDMEDLINE is covered back to 1950.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2006 vocabulary.

This file contains CAS Registry Numbers for easy and accurate substance identification.

FILE BIOSIS
FILE COVERS 1969 TO DATE.
CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 10 May 2006 (20060510/ED)

FILE EMBASE
FILE COVERS 1974 TO 16 May 2006 (20060516/ED)

EMBASE has been reloaded. Enter HELP RLOAD for details.

EMBASE is now updated daily. SDI frequency remains weekly (default) and biweekly.

This file contains CAS Registry Numbers for easy and accurate substance identification.